

The use of a robotic device for upper limb retraining in subacute stroke

Thesis submitted in fulfillment of the requirements for the
degree of Doctor of Philosophy

KAREN BAKER

Institute of Neurology
University College London

Word Count:

Thesis: 67,486

Appendices (including bibliography): 17,892

I Karen Baker, confirm that the work presented in this thesis is my own. Where information has been derived from other sources, I confirm that this has been indicated in the thesis.

ABSTRACT

Stroke is a significant cause of disability in the population. When the arm is affected by stroke, functional recovery may be poor. The use of robotic aids to enhance arm recovery is a novel treatment adjunct. There is a growing support for using robots as an adjunct to therapy but there has been little translation from research into clinical use.

The investigations reported in this thesis aimed to bridge the gap between research and clinical use of these devices. To achieve this, five stages were carried out:

Firstly a systematic literature review of outcomes measure used for the upper limb was conducted to establish the most reliable, valid and responsive scales. This review found a battery of measures (ABILHAND, CHAI, STREAM, FMA, ARAT, EQ5D, DASH, NIHSS).

An evaluation of 125 consecutive acute stroke patients established the proportion of patients that potentially benefited from rehabilitation using a robotic device. This found that around 50% of subjects could use a robotic aid and that it was practically feasible to carry out the intervention.

A pilot RCT performed on 37 participants using the battery of measures found a significant difference with use of the robotic device on the ABILHAND, This was not seen with the other measures, however there was a trend towards improvement in motor performance and function in the robotic group. In depth interviews with participants found subjects perceived gains with using the robot but fatigue stopped them using it for longer periods.

Psychometric analysis of the outcome measures used found difficulties with the instruments in reflecting clinically change.

The studies showed that a robotic device could be used practically; however stratifying subjects into arm severity would help provide further information over who could benefit from the intervention. Identifying appropriate ways of measuring changes that are clinically meaningful would also be beneficial.

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ACKNOWLEDGMENTS

FOR THE SUPERVISION OF THE PHD PROJECT:

Dr Diane Playford who provided advice, assistance, mentoring and supervision and who without this would have never been possible.

FOR ADVICE AND ASSISTANCE:

Dr Amanda Wallace, Dr Trefor Asfden, Dr Asfane Riazi, Brid Spillaine, Dr Stefan Cano, Dr Joanne Sweetland, Dr Gail Eva

DATA COLLECTION

Kevin Ohara who supervised each subject on ReachMAN

FUNDING

UK Stroke Association, NHNN Therapy and Rehabilitation (Education funding), CSP (Educational funding)

AUTHOR CONTRIBUTION

All Chapters were the sole work of the author. In accordance with UCL rules it is important to indicate where information has been derived from other sources:

- The design for the studies was established by Dr D Playford before the author joined the research team in 2008
- pReachMAN and ReachMAN robotic devices were designed and built by Alejandro Melendez and Che Fai Yeong
- Stefan Cano and Diane Playford advised on the Scale Selection paper that Chapter Four is based on
- Interviews described in Chapter Seven were carried out by Brid Spillane (are also included in her Msc for Brunel University)
- Processing and Rasch analysis of the data in Chapter Eight was undertaken by the author and Dr Trefor Asfden. Dr Afsane Riazi advised on Rasch and the traditional psychometric analysis

PERSONAL SUPPORT

This thesis would not have been written without the support of Marc Yacobi and Dr William Baker. I cannot express my gratitude to both enough. Thank you also Eva and Aron for letting mummy work.

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Baker K, Cano SJ, Playford ED. Outcome measurement in stroke: a scale selection strategy. *Stroke* 2011; 42(6):1787-1794.

Yeong CF, Melendez A, Burdet E, **Baker K**, Playford ED. ReachMAN to help sub-acute patients training reaching and manipulation in Proceedings 2010
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List of Abbreviations

Abbreviation:	Meaning:
TIA	Transient Ischaemic Attack
ICH	Intracerebral Haemorrhage
DALYs	Disability adjusted years
NHS	National Health Service
SAH	Sub Archnoid Haemorrhage
ADL	Activities of Daily Living
CIMT	Constraint induced movement therapy
NMS	Neuromuscular stimulation
MIME	Mirror Image Movement Enabler
MRI	Magnetic Resonance Imaging
BFIAMT	Bilateral force-induced isokinetic arm movement trainer
FMA	Fugl Meyer upper limb assessment scale
PROMS	Patient Reported Outcome Measure
FIM	Functional Independence measure
CT	Computerised Tomography
PhD	Doctorate of Philosophy
NAO	National Audit Office
UK	United Kingdom
RCT	Randomised control Trial
ARAT	Action Reach Arm Test
REHAROB The Disabled	Robotic Rehabilitation System for Upper Limb Motion Therapy for
NeReBot	Neuro-Rehabilitation Robot
HWARD	Hand Wrist Assistive Rehabilitation Device

CHAPTER 1 BACKGROUND AND LITERATURE REVIEW

1.1 INTRODUCTION

Robotic aids may enhance upper limb motor recovery after stroke through repetitive, task-specific training. There is a growing research regarding the use of these aids as an adjunct to therapy. However unanswered questions remain, especially as currently the use of these devices have had little integration into clinical practice.

This thesis describes studies which aim to address some of the gaps in the current literature particularly around the practical implementation of this novel therapy. The research presented in this thesis was completed between 2008 and 2011.

A broad overview of the literature relating to stroke, the upper limb, and specifically its recovery after stroke is presented in this chapter (Chapter One). This chapter also considers the types of therapy intervention for the upper limb after stroke. Chapter Two then presents a specific literature review on the use of robotic devices in upper limb rehabilitation. The aims, research questions, and hypotheses are set out in Chapter Three of the thesis.

The original research is in four parts. Firstly, a systematic literature review was completed to establish the most appropriate upper limb outcome measures to evaluate upper limb recovery with use of a robotic device. This is described in Chapter Four. A recruitment trial (Phase I study) to evaluating the amount of participants who could potentially use the device and define inclusion and exclusion criteria technique was completed in an acute stroke population. Details of this are given in Chapter Five. A preliminary Randomised Control Trial to evaluate the effect of a novel robotic device (ReachMan) is described in Chapter Six. A quantitative study to investigate participants perception of the robotic device was carried out in parallel to the RCT and is described in Chapter Seven. A psychometric analysis of the outcome measures used in the study was performed and a detail description of this for two of the measures used is given in Chapter eight. Finally, these interrelated strands are brought together in the discussion (Chapter nine) and conclusions of this thesis.

1.2 BACKGROUND AND LITERATURE REVIEW

This chapter will firstly present a background and literature review on stroke. The aim is to place the research initially in a broader context, by discussing the nature and impact of stroke. This chapter will provide an introduction to the effects of stroke on individuals, and current theories of brain reorganisation will be discussed. Specific emphasis on the impact of stroke on the upper limb and recovery of the upper limb will be considered. The theoretical underpinning of the therapies that are employed in stroke rehabilitation will also be discussed. This will provide a background into the development of using robotic devices as a novel therapy adjunct in upper limb rehabilitation.

1.3 STROKE

1.3.1 DEFINITION

Stroke has been described as a “Brain Attack” ¹. This definition has been used in the National Stroke Strategy ¹ to signify that stroke is a medical emergency requiring immediate attention. Stroke is due to the loss of blood supply to a part of the brain in a similar way that the loss of blood supply to the heart muscles leads to a “heart attack”. The definition of stroke given by the World Health Organization is, “rapidly developing clinical signs of focal (or global as in coma or subarachnoid haemorrhage) disturbance of cerebral function, lasting more than 24 hours or leading to death with no apparent cause other than vascular origin” ².

Blood supply to the brain may be disrupted in one of two ways: either a thrombus formed in situ or originating elsewhere blocks a blood vessel (ischaemic stroke), or a blood vessels ruptures (haemorrhagic stroke). The type of stroke can be reliably determined only by neuroimaging ³. The results of this disruption of blood supply is that an area of brain tissue is rendered inactive or may die. The volume of brain tissue affected together with the lesion location will govern the nature, severity and duration of symptoms. Another source of variation in the impact of stroke is the fact that precise details of brain architecture will vary between individuals. Stroke is therefore an extremely heterogeneous condition. Any aspect of brain function may be affected by stroke; and the physiological and psychological responses to the damage are wide ranging making it difficult to generalise about the stroke population. The heterogeneity of the condition also makes the

identification of appropriate treatments and research into the efficacy of these treatments problematic, as a treatment that works well for one person may be ineffective for another .

Where the symptoms of a stroke last less than 24 hours the event is described as a Transient Ischaemic Attack (TIA or 'mini-stroke')⁴. This is often the forerunner of a more major event, with a 20% risk of a full stroke within four weeks of a TIA ⁴.

The use of the terms acute, sub-acute and chronic in reference to time elapsed since stroke are not used consistently in the literature. In view of this the definition of the terms used in the Royal College of Physicians' guidance⁵ will be assumed throughout the thesis:

- Acute (or early): the period up to seven days after stroke
- Sub-acute: one to 26 weeks after stroke (first six months)
- Chronic: six months or more after stroke

1.3.2 EPIDEMIOLOGY

The National Audit Office (NAO) ⁶estimates that 110,000 strokes and 20,000 TIAs occur in England each year. Stroke is now the second most common cause of death globally⁷ , and accounts for 9% of death in England each year⁶ Feigin et al (2014) ⁹ note that international stroke mortality rates have declined in recent years, the absolute number of people who have a stroke every year, stroke survivors, related deaths, and the overall global burden of stroke (DALYs lost) are great and increasing. A study by Lee et al (2011)¹⁰ reports that incidence and mortality rates for stroke in England have decreased over the ten years between 1998-2008, with the incidence of stroke in the UK falling by 29%. Lovelock et al ¹¹ analysed the incidence of intracerebral haemorrhage (ICH) in the population of Oxfordshire over a 25 year period. They found that although ICH related to hypertension reduced over the period, incidence of ICH in older people had increased possibly due to an increase in the use of antithrombotic drugs. They suggested that the incidence of ICH may therefore increase with the ageing population. Feigin et al (2014) ⁹ in a global systematic review spanning 40 years, found a non-significant reduction in ICH in developed countries , whereas the incidence of subarachnoid haemorrhage had remained stable.

Stroke occurs in all age groups, but primarily affects older people, with three quarters of all first strokes occurring after the age of 65⁸. Bonita(1992)¹² reports that almost one in four men and one in five women aged 45 can expect to have a stroke if they live to 85.

Prevalence (number of people with stroke at a given time) was calculated by Feigin et al (2013)¹³. Data from nine studies gave a range of the prevalence for people over 65 years between 46.1 and 73.3 per 1000 population (men 58.8 to 92.6: women 32.2 to 61.2).

1.3.3 BURDEN OF STROKE

There are significant personal, social and health costs associated with stroke. There are more than a million people living with the consequences of stroke in the UK.¹⁴ It is estimated that half of these individuals are dependent on others for everyday activities⁶. Stroke has been reported to be the seventh leading cause of disability-adjusted life years (DALYs) in the developed world² and fifth in the developing world.¹⁵ The National Stroke Strategy¹ reports that stroke is the single largest cause of adult disability in the UK.

The accurate diagnosis, investigations and management of stroke should lead to a better outcome for individuals affected³. The National Stroke Strategy¹ has been adopted in the UK with the aim of preventing stroke and treating strokes more effectively. Not only is there a moral imperative to provide optimum prevention and after care, but it also makes economic sense. It is estimated that stroke costs the NHS and the economy about £7 billion a year: £2.8 billion in direct costs to the NHS, £2.4 billion of informal care costs (e.g. the costs of home nursing borne by patients' families) and £1.8 billion in income lost to productivity and disability⁶. These statistics underlie the major cost to individuals with stroke in terms of lost independence, and to their families and communities in respect to the assistance that stroke survivors need in the long term.

1.3.4 AETIOLOGY

Strokes are caused as a result of blood vessel occlusion, hence the main risk factors for stroke are also risk factors for atheroma and heart disease¹⁶. Warlow et al (2003)¹⁷ estimated that in the white population, half of all ischaemic strokes are due to arteriothrombotic disease, a further 20% being caused by emboli arising from the heart, and approximately 25% being due to occlusion of one of the deep perforating arteries

leading to lacunar stroke. There is a steeper relation between stroke and blood pressure than for ischaemic heart disease ¹⁷ , with 65% of people with stroke having hypertension¹⁰. In contrast with heart disease there is no proven association between plasma cholesterol concentrations and stroke. The main risk factors for stroke are illustrated in Table 1.1. Strokes are usually the result of a combination of risk factors coming together rather than any single one ¹⁶

Table 1.1: Major risk factors of stroke age

Hypertension
Smoking
Diabetes mellitus
Atrial fibrillation
Heart disease
Dyslipidaemia
Alcohol
Obesity
Symptomatic and asymptomatic carotid stenosis
Drug misuse
Adapted from Losseff et al (2009) ¹⁶

1.3.5 DIAGNOSIS OF ACUTE STROKE

Acute stroke is a medical emergency and the longer treatment is delayed, the less scope there is for benefit from treatment (leading to the term “time is brain”.) The main form of diagnosis is via clinical questioning and assessment. However, Ricci et al (1993) ¹⁸ found that in general medical and emergency department settings up to 20% of patients with suspected stroke turned out to have another diagnosis. Brain imaging is the only reliable method to distinguish a haemorrhage from an infarct ³ and this distinction is important as treatment such as aspirin and thrombolysis are dangerous to give when haemorrhage has occurred. In 2005, NAO (2005)⁶ found that less than 20 per cent of stroke units had access to scans within three hours of admission. This led to the National Stroke Strategy ¹ calling for an overhaul of stroke services in the UK to enable immediate transfer to a hospital with 24 hour hyperacute services. London now has eight hyper-acute stroke units treating all stroke patients in the first 72 hours after a stroke. These units provide expert

triage, clinical assessment, urgent brain imaging, intravenous thrombolysis if appropriate and prompt access to acute stroke unit and early multidisciplinary assessment.

Furthermore, admission to a hyperacute unit can allow investigation and treatment of high-risk patients with TIA within 24 hours which could produce an 80 per cent reduction in the number of people who go on to have a full stroke ¹. A recent study investigating the impact of this centralized approach to acute stroke care in London found a reduced mortality for a reduced cost per patient, with these hyperacute units¹⁹.

1.3.6 MANAGEMENT OF ACUTE STROKE

Stroke was seen as untreatable, however over the last 20 years this has changed to being seen as a condition where there is now a range of options for acute interventions, which have been shown to improve outcome ¹⁶. Intensive physiological and neurological monitoring in the early phase of a stroke supports early treatment that halts stroke progression and prevents more brain cells being damaged ¹. In the first few hours after stroke, measures are designed to restore blood flow (reperfusion), preserve the ischaemic penumbra (neuroprotection) and prevent early recurrence (aspirin treatment) ¹⁶.

Three main Cochrane reviews have supported three interventions for acute stroke care: organized stroke care²⁰, early administration of aspirin for almost all patients with acute ischaemic stroke²¹, and intravenous thrombolysis for select patients with acute ischaemic stroke.²² A recently updated Cochrane Review ²⁰ included a meta-analysis of studies of stroke unit care and strongly supported them for acute treatment. It concluded that the numbers needed to treat to get one additional “good” outcome were low (33 for survival, 20 to regain independence and 20 to return home). Two large randomized trials have shown that aspirin, given within 48 hours of onset, has a small but significant benefit in reducing the rate of recurrent ischaemic stroke^{23;24}. Although this benefit appears small, in the UK it is estimated that if everyone in the UK with stroke were given aspirin with 48 hours of onset (after CT scan to exclude haemorrhage), then more than 1000 people would be saved from death or disability every year ¹

Thrombolysis therapy is a novel development in stroke medicine and is not without controversy²⁵ The thrombolytic or “clot-busting” drug alteplase (rt-PA) has been tested in clinical trials in ischaemic stroke since the 1990s The NINDS study²⁶ showed that one in

eight people benefited from being thrombolysed within three hour onset of symptoms, making a full or nearly full recovery. Treatment was associated with a chance of fatal intracranial haemorrhage and treatment was in highly selected patients²⁶. Guidelines vary as when to administer the drug due to limited trial evidence. The IST3 trial ²⁷in May 2012 found that thrombolysis within 6 h improved functional outcome. This benefit did not seem to be reduced in people who were over 80 years old. In the UK, recent reports illustrate that the thrombolysis rate has increased from 1.8% in 2008 to 5% nationally in 2010⁵. The Department of Health has suggested that if this were increased to 10% over 1,000 people would regain independence rather than die or be severely impaired²⁸. The NAO ²⁸ estimated that the net saving to the Health Service of implementing this would be £16 million per annum.

Physiological abnormalities including increased temperature, low blood oxygenation, altered blood pressure and high blood sugar levels often occur after stroke¹⁷. Within the setting of a stroke unit, patients are monitored closely and appropriate interventions are given to prevent or treat those physiological abnormalities and other complication ²⁹

At present rehabilitation, rather than, say, drug treatment is the main strategy for driving recovery after stroke. The great promise of many pharmaceutical interventions (such as amphetamines) has yet to be realized ³⁰. A recent study investigated the use of fluoxetine with physiotherapy suggested enhanced motor recovery after 3 months, however further work is needed to investigate the effect of this drug treatment. ³¹This is in sharp contrast to the striking benefits seen with techniques such as brain care (described above) and thrombolytic therapy whose primary aim is to prevent damage from occurring in the first place. A study from Canada ³² investigated over a five year period at the impact of thrombolysis on progress through inpatient rehabilitation, found no evidence to suggest that it contributes to greater functional improvement.

1.3.7 EFFECTS OF STROKE (GENERAL)

A significant proportion of those who have a stroke will die within the first month. Feigin et al (2009) ⁸ report that the case fatality ranged from 17% to 30% (25-35% ICH, 25-35% SAH and 13-23% in ischaemic stroke) in high-income countries. Much higher percentages of deaths occur early post stroke in people who have had haemorrhages in low-income

countries (30-48% ICH, 40-48% SAH). Warlow et al (2003)¹⁷ suggest that death immediately after stroke is most often due directly to the brain lesion, either causing a mass effect or disrupting vital centres. Death occurring later are likely to be due to complications such as pulmonary embolism or infection ³³.

However, as most patients with stroke survive the initial injury, the biggest consequence on patients and family is usually through long-term impairment, limitations of activities and reduced participation⁷. Lawrence et al (2001)³⁴ reported the prevalence of acute impairments in a large population of first-ever strokes. Table 1.2 lists the most commonly occurring deficits as seen in this study. A recent sentinel audit⁵ also reported similar prevalence of impairments

Table 1.2: Impairments associated with stroke

Impairment	% of the stroke population affected
Upper limb weakness	77.4
Lower limb weakness	72.4
Urinary incontinence	48.2
Impaired consciousness	44.7
Dysphagia	44.7
Impaired cognition	43.9
Dysarthria	41.6
Upper limb sensory deficit	30.3
Lower limb sensory deficit	27.2
Visual field neglect	26.1
Dysphasia	23.0
Visual neglect	19.8
Sensory inattention	19.4
Gaze paresis	18.4
Ataxia	7.23
Deficits that are independently associated with death and severe disability at three months after stroke. Data taken from Lawrence et al (2001) ³⁴	

As is clear from the above data, the most common and widely recognised impairment caused by stroke is motor impairment. However other important functions may be affected by stroke.

Neglect primarily affects those with right hemisphere lesions ³⁵. A range of features may be present with either sensory or motor systems, or both, being affected. Spatial neglect has visual and non-visual components, affecting extrapersonal and/or personal space. Neglect may also be linked to attention deficits ³⁶, and may impair an individual's ability to engage in rehabilitation activities leading to a poor prognosis ³⁷.

Sensory loss or diminution of sensory perception may also be caused by stroke. The detection of pain, temperature, touch or proprioception may be affected, and the interpretation of sensory information (eg stereogenesis, textual discrimination), may be impaired ³⁸. Altered sensory perception may have a detrimental impact on an individual's ability to use their arm and so impede recovery. For example, in a study of upper limb recovery, Feys et al (2000) ³⁹ found that proprioceptive loss was prognostic of poor outcome.

Cognitive deficits resulting from stroke can have devastating impact on both patients and their families ⁴⁰. Studies report that up to 65% of stroke survivors demonstrate new onset or worsening of cognitive impairments after stroke ⁴¹. Stroke-related cognitive deficits interfere with functional recovery and may influence an individual's ability to engage in rehabilitation.

Other functions such as swallowing, communication, perception, depression, fatigue and continence may be affected by stroke and again can interfere with functional recovery and the potential benefits of rehabilitation.

All the above impairments can impede on the rehabilitation process and impact on the potential for recovery. This thesis will now, however focus specifically on the upper limb post stroke.

1.3.8 PHYSICAL EFFECTS OF STROKE ON THE UPPER LIMB

Motor deficits of the upper limb following stroke may range from total paralysis to partial paresis. Authors ^{42;43} suggest that there are three main components of compromised motor control following stroke these include: weakness, impaired inter-segmental coordination, and hyperreflexia or spasticity:

Muscle weakness in the upper limb after stroke may be due to alterations in neural drive as a result of supraspinal changes to the alpha motor neuron pool at a spinal segmental level, structural changes and atrophy in skeletal muscle in response to impaired muscle activity and reduced activity can also cause weakness. In addition the stroke population tends to be older in age and so will also have normal muscle changes associated with older age. This may compound on any effects of the stroke. There is a growing body of evidence that suggests that weakness plays a significant role and contributes directly to compromised motor function post-stroke^{43;44} Canning et al(2004) ⁴⁵ and Harris and Eng (2007), ⁴⁴ for example, found that loss of strength is a major contributor to physical disability following stroke, and Shelton et al(2001) ⁴⁶ found a significant relationship between the severity of motor impairment and functional recovery.

Impaired inter segmental co-ordination has been extensively described⁴⁷⁻⁴⁹ Causes for this are likely to be multifactorial: there may be contributions from a decrease in pre-synaptic and reciprocal inhibition^{50;51}, reorganisation at cortical or spinal level in response to lesion⁵², change in the descending pathway used to carry the signal to move^{53;54} and alterations in stretch reflex threshold ⁴⁷may also contribute. Impaired co contraction has particularly been described around the shoulder and elbow joints during attempts to reach^{47;55}. Authors comment that subjects are constrained to a smaller number of stereotypical movement patterns, particularly after severe stroke, with abnormal patterns such as unwanted elbow flexion, with shoulder abduction or forward flexion^{55;56}. There is much debate in the literature to the extent which co contraction is a separate phenomenon from spasticity^{47;56}

The most common definition of spasticity is that by Lance (1980)⁵⁷ as “a velocity-dependent increase in tonic stretch reflexes with exaggerated tendon jerks, resulting from hyper-excitability of the stretch reflex” With the growing body of evidence into spasticity this definition is argued to be not fully accurate and does not reflect the clinically presentation of spasticity. ⁵⁸

Pandyan and colleagues (2005)⁵⁹ argue that spasticity is not a pure motor disorder and is not caused solely by hyper-excitability of the stretch reflex. They propose the following broader definition of spasticity: "Disordered sensori-motor control, as a result from an upper motor neuron lesion presenting as intermittent or sustained involuntary activation of muscles."

It is difficult to measure and scales exist for the assessment of muscle tone; however, the reliability and validity of these have been contentious^{60,61}. In a study of the cause of contractures after stroke, Ada et al (2006)⁶², found that spasticity was the major contributing factor to the development of contractures in the first weeks after stroke, but that after four weeks weakness was the most significant factor.

Sensory modalities (e.g. pain, temperature, proprioception, vibration, light touch) can be affected by stroke and the loss may be partial or complete,³⁸ Sensory deficits can have a profound impact on the function of the limb⁶³. In addition to the loss of sensory input, the interpretation of sensory information (e.g. stereognosis) can be affected by stroke and this may cause a reduction in function⁶⁴.

Stroke may cause a range of types of perceptual neglect. In such cases, an individual may have a poorly functioning arm and hand, despite good muscle strength, due to poor awareness of its existence⁶³. Additionally, neglect can lead to mechanical trauma as the limb may be kept in a poor position. This may result in further complications, including pain and apraxia.

The prevalence of shoulder pain has been described as well-known impairment after stroke⁶⁵. The incidence of upper limb pain has been reported to vary widely from 9% to 40%. Some prevalence estimates as high as 84%.⁶⁵ There are multifactoral reasons for shoulder pain: Mechanical damage (e.g. shoulder subluxation) may be a secondary consequence of stroke, which can lead to shoulder impingement⁶⁶. Pain can also be of central origin and, as with mechanical pain, may lead to protection and disuse of the limb⁶⁷. Post stroke shoulder pain contributes to longer hospitalization times⁶⁶ and is associated with depression⁶⁸ and decreased quality of life⁶⁹. Loss of or a reduction in arm motor function at the onset of stroke or during the rehabilitation phase have been shown to be predictors of the development of poststroke shoulder pain^{70,71}. Shoulder pain also has been reported to be more frequent or intense among persons with left-sided hemiparesis⁷²

⁶⁵. Reduced shoulder ROM in the hemiparetic side of persons with shoulder pain is observed within the first weeks after the onset of stroke ⁷³ and tends to worsen during the first months^{65;73}

1.3.9 RECOVERY POST STROKE

Recovery of function after stroke is variable and depends on the nature and extent of the stroke and the characteristics of the individual affected, such as pre-existing impairments and co-concurrent disease. Early recovery following stroke is understood to be due to the resolution of cerebral swelling, reperfusion of the ischaemic penumbra and gradual reversal of diaschisis⁷⁴. Later recovery is believed to be due to capacity of the brain for reorganisation of neural networks (neuroplasticity) in response to the damage and behavioral compensation (including those encountered in rehabilitation) ^{75;76} and And activity dependent plastic change

The impact of a person's age (as opposed to age-associated co-morbidity) at the time of stroke, on recovery is controversial. Black-Schaffer and Winston (2004)⁷⁷ performed a study involving almost 1,000 people looking at the effect of age on outcome. They found that in the higher functioning subjects (Functional Independence Measure (FIM) score of over 80) age did not predict outcome. The older subjects in this group achieved the same functional gains as the younger cohort. In the more impaired group the older subjects did not make as good a functional recovery by discharge as their younger counterparts. The authors suggest that recovery may be as good in this group in the longer term but that they may need a longer period to reach the same point.

There are three neuroplastic phenomena that occur in the nervous system following a lesion, which facilitate structural and functional reorganisation^{78;79}. These include denervation super sensitivity, collateral sprouting and unmasking of silent (latent) synapses.

Denervation super sensitivity occurs when there is a loss of input from some brain regions. An increased release of transmitter substances causes a heightened response to stimulation. ⁸⁰ Post-synaptic target neurons become hypersensitive to the transmitter substance, increasing the number of receptor sites. Collateral sprouting appears in the cells surrounding the lesion, where collateral dendrites make connections with those synapses lost by cell necrosis .⁸¹ Experiments in animals have found unmasking of silent

synapses occurring when previous non-functioning neurons are accessed to form new connections.^{82 83} These studies have also found that changes within the structure of the nervous system can be organised or disorganised producing adaptive or maladaptive sensorimotor behaviour, which can promote or be detrimental to recovery.^{76;84}

In addition to neural reorganisation, individuals may employ compensatory strategies to maximise their function. Enriched environments giving subjects greater than normal stimulation has been shown, at the right time, to promote significant neuroplastic changes and improvement in functional outcomes.^{85 86}

Although many of the studies that have contributed to the current understanding on neuroplasticity have come from animal studies, it is likely that the complex interconnections of the human brain are disrupted in a similar way to those of primates⁸⁷. Brain imaging studies support Nudo^{76;84} and others work. Baron⁸⁸, for example, describes the expansion of areas of the Primary Motor Cortex (M1) adjacent to a stroke, possibly due to the unmasking or disinhibition of latent connections or recruitment of areas not normally associated with the function. Plasticity may be influenced by behaviours and it has been postulated that early repetitive practice of any task may be associated with improved outcome due to plasticity.⁸⁹

Ward (2011)⁹⁰ reports that in the early stages after stroke sensorimotor tasks using the paretic arm and hand lead to activation in many areas of the brain, including the primary motor, premotor and supplementary motor cortices of both hemispheres. People who have poor recovery continue to demonstrate this diffuse pattern of activation, whereas those with better⁹¹ recovery show a more normal pattern, usually limited to the ipsilesional hemisphere.

1.4 UPPER LIMB RECOVERY

Upper limb recovery after stroke is still unacceptably poor⁹². Reports in the literature vary as to the proportion of patients who actually recover upper limb function. Gowland et al (1982)⁹¹ investigated the prognosis outcome of 223 stroke patients. They found that only 5% of the patients regained arm function. Dean and Mackey (1992)⁹³ however reported that 52% of subjects they studied regained upper limb function. Broeks et al (1999)⁶⁷

found a similar percentage (50%). Kwakkel et al ⁹² however found only 11.6% of the stroke subjects they investigated gain upper limb functional use. These longitudinal studies all used different sample sizes, inclusion criteria, durations of treatments and outcome measures. However regardless of these differences, these studies all indicate a poor recovery of arm and hand use following stroke. This is seen even more so in comparison to the number of patients who gain lower limb recovery and the ability to walk, with studies reporting 70/80% of patients being able to walk ^{17,93} Although, the lower limb recovers more completely than the upper limb, clinically there is interdependence between the upper and lower limb. ⁹⁴ An improvement in the ability to use the upper limb in a reach task is linked to the ability to use the lower limb for support and balance. ⁹⁵

It is hard also to define what constitutes “good recovery” in the upper limb post stroke. Studies that have found improvement in arm function at an impairment level do not necessarily directly link to a functionally meaningful change.^{96,97} Winstein et al (2003) ⁹⁷. comment that the relationship between impairment, participation, and activity limitation are complex and affected by numerous modifying factors.. People with stroke themselves have reported difficulties with arm movements, although they were measured clinically as having no arm impairments ⁹⁶ Furthermore studies ^{67,97} have also suggested that functional motor recovery of the UL tends to occur later in the rehabilitation period.

1.4.1 REASONS FOR POOR UPPER LIMB RECOVERY.

There is no clear evidence that identifies the reasons for the poor recovery of the arm following stroke, although a number of theories have been identified. To place these in context, it is helpful to explore the functions and use of the arm in everyday tasks.

1.4.2 THE UPPER LIMB

The hand and arm have an extensive range of functions, including the movement and manipulation of objects; communication and expression through gesture and touch; tactile sensation and exploration; and aiding balance and locomotion. In terms of manipulation, the unique flexibility of the human hand (especially as provided by the opposable thumb) allows a myriad of both power and precision grips. Although other species are able to use their hands to hold objects, their manipulative ability is compromised by the need for the limb to be involved in locomotion ⁹⁸.

The range of movement provided by the shoulder complex, elbow, radio-ulnar and wrist joints allows the upper limb to reach objects at some distance from the body and in many directions. Stability at the trunk and around the joints is important to enable the transport of objects and this is provided primarily by muscles and ligaments ⁹⁸. The joints of the upper limb act as a complex to reach and manipulate objects. Grip is shaped as the hand is transported towards an object ⁹⁹. The position of the digits is adjusted during reaching to provide a grasp shaped to allow the target to be encompassed. The forces coordinated by the hand are coordinated with those of the arm in order to lift and transport the object. There are a remarkable number and range of grips available which have been documented in detail by a number of authors ^{100 101}, in general they are classified as power grips and precision grips. Although standard grips have been described, each individual may use idiosyncratic or improvised grips, and actions may not always be completed in the same way ⁹⁸. Additionally, dominant and non-dominant hands may be specialised for different tasks: for example the dominant hand is often used for more precise actions and non-dominant for stabilising or supportive actions ⁹⁴.

When reaching for an object it can be observed that the path along which the hand moves usually approximates a straight line between start and end points. This requires simultaneous coordination of changes in angles of wrist, elbow and shoulder joints and takes into account kinematic factors and torques. Morasso (1981) ¹⁰² in a "Manipulandum Study" found that spatial paths had straight lines and the velocity profile had a smooth single peaked form regardless of direction. The functions of the hand and arm are as much sensory as motor⁹⁴, tactile and pressure sensors provide precise information about the texture, temperature, shape, size and weight of objects. This allows us to distinguish between different shape and size coins without looking and objects in the dark. The hand acts as an exploratory sensory organ in that it can move towards, or seek out, stimuli, unlike the eye or ear which merely responds to stimuli reaching them ¹⁰³.

The hand and arm are also used as a means of communication. Touch and gesture convey a variety of messages to others and provide a means to demonstrate emotion (such as a slap or a shaken fist, thumbs up), a sign (beckoning, waving) or a command. Paralinguistic signs also accompany speech.

The arms are involved in posture, when balance is compromised, the arms play a stabilizing and supportive function and if balance is lost, the hands are used to form a new

base of support⁹⁴. Postural adjustments occur prior to during arm movements and this has been reported to occur when reaching for objects in standing, sitting and pointing⁹⁴.

Most commonly performed activities are performed bimanually (such as feeding, dressing, brushing teeth and washing). This involves complex interactions between the two limbs with co-ordination of both. Consequently, the implications of not being able to use an arm following stroke has broader implications. The inability to feed oneself or to use utensils in an appropriate way, and require assistance to wash and dress can be socially incapacitating and may also be embarrassing or humiliating.

The aging process causes “normal” changes to occur in reaching, grasp and manipulation¹⁰⁴. Reaching movements have been found to be slower in over 65 and this is thought to relate to slowness in central processing, with slowing in performance on reaching movements being greater for complex tasks than simpler ones⁹⁴. Carmeli et al 2003¹⁰⁴ report a decline in hand function after the age of 65 and relate this to changes in the musculoskeletal, vascular and nervous systems. Grip strength decreased with increased age¹⁰⁵ and sensory thresholds increase¹⁰⁶. These “normal” changes may also be accompanied by other pathologies such as osteoarthritis which may also affect hand function. As stroke predominantly affects the older population, these “normal” age related changes are likely to be present in many people prior to their stroke.

1.4.3 SUGGESTED THEORIES FOR THE REASONS FOR POOR UPPER LIMB RECOVERY.

Multiple causes may explain poor recovery in the upper limb and this will now be explored. They include:

- Complexity of upper limb function
- Site and size of the lesion post stroke
- Learned non use
- Secondary complications
- Hand dominance
- Amount of time spent on upper limb rehabilitation.

1.4.4 COMPLEXITY OF UPPER LIMB FUNCTIONS

As described in section 1.4.2, the upper limb is involved in an extensive range of functions. Desrosiers et al (2003)¹⁰⁷ suggest that functional motor recovery of the UL tends to occur later in the rehabilitation period. This may be due to the greater degree of sensory integration and fine motor control required for manual dexterity rather than gait. This may also be a contributing factor to the poorer functional recovery seen in the upper limb following stroke. Broeks et al(1999)⁶⁷ report that patients four years after stroke described loss of arm function to be a major problem, despite their being assessed in standard tests as having “reasonable” upper limb function. While patients can walk with relatively large lesions and impairments, a functioning upper limb requires a greater degree of improvement, as it comprises a complex integration of muscle activity^{108 109}

1.4.5 SITE AND SIZE OF THE LESION POST STROKE

The size and site of the lesion post stroke has been postulated as a possible reason for poor recovery in the upper limb post stroke. The higher prevalence of Middle Cerebral Artery (MCA) than Anterior Cerebral Artery (ACA) stroke, may explain the greater proportion of patients in whom the arm is more severely affected than the leg¹¹⁰

Shelton and Reding (2001)⁴⁶ found in a study of 41 stroke subjects that recovery of the upper limb was more likely by the time of discharge in those with purely cortical strokes (supplementary motor area (SMA), premotor area (PMA) or motor cortex (MI)) rather than those with strokes in either the corona radiata or internal capsule. They propose that subcortical strokes may have a devastating impact on function as they affect the descending motor pathways as they converge to leave the brain, so that more fibres can be damaged. Feys et al (2000)³⁹ et al found a similar correlation between lesion location and recovery at 2 months after stroke, in 45 subjects. They found that recovery at twelve months was found to be predicted more accurately by clinical tests of motor activity. Feys et al ; (2000)³⁹ noted that recovery tended to be slower in the case of subcortical strokes. This may explain the finding of Shelton and Reding (2001)⁴⁶ whose final outcome was on discharge (with an average length of stay of 62 days). Schiemanck et al (2008)¹¹¹.and Puig et al (2011)¹¹² found similar associations with poorer arm function with more loss of ipsilesional tract integrity at the level of the posterior limb of the internal capsule.

Numerous studies propose that a patient has better prospects for upper limb recovery if TMS can elicit motor-evoked potentials (MEPs) in affected upper limb muscles within the

early days of stroke¹¹³. Although, some individuals with no upper limb MEPs may still recover some manual dexterity¹¹⁴. Using TMS, together with the use of brain imagery findings have led to studies predicting the potential for upper limb recovery in the early days post stroke^{113;115}. These studies are however preliminary in nature, using a small number of patients and have used patients lacking cognitive difficulties.

Corticospinal tract integrity (as measured by Diffusion Tensor Imaging) has been seen to be a key prognostic indicator. Stinear et al (2007)⁵⁴ found that functional potential in chronic stroke patients was dependent on corticospinal tract integrity. Subsequent work^{112 116} have also found this to be true.

1.4.6 LEARNED NON-USE

From the earliest stages after a stroke, an individual will adapt to the changes brought about by it. This may be seen in the assumption of new postures or in the use of a non-dominant hand to complete functional tasks. This compensation for loss of function is likely to drive neural reorganisation and lead to the reinforcement of the pathways that support compensatory movements¹¹⁷. In some cases this will interfere with recovery of normal function. Taub et al (1999)¹¹⁸ considers that people with stroke may develop 'learned non-use'. It is proposed that some of the decrease in hand and arm function after stroke is not directly related to impairments such as loss of muscle strength. Instead, it is suggested, repeated failed attempts to use the hand and arm lead to the individual adopting movement strategies that do not involve the affected limb¹¹⁸. This would result in weakness due to non-use and therefore further limit the use of the limb. Sunderlad and Tuke (2005)¹¹⁹ question whether 'learned non-use' is merely that the difficulty of using the affected limb leads to a preferential use of the other limb, despite an ability to use it. This could be an adaptive response brought about by choice not to use the limb.

1.4.7 SECONDARY COMPLICATIONS

However, other impairments such as spasticity, sensory deficits, spatial neglect, cognitive impairments, dyspraxia, and ataxia also impact on the functional ability of the UL. (These have been described in more detail in sections 1.3.7). Secondary effects such as soft

tissue shortening, pain or learned non-use (discussed above) may also result in reduced UL function.

1.4.8 HAND DOMINANCE

Hemisphere dominance is an extensive and complex topic which is beyond the scope of this thesis. However, it is important to note that it may be a factor affecting upper limb function after stroke. In many individuals a strong preference for the use of one hand is apparent, and the functional uses of the dominant and non- dominant hands differ ¹²⁰. This may influence an individual's motivation for using the affected limb.

1.4.9 TRUNK AND UPPER LIMB POSTURAL CONTROL

Efficient control of posture is important for upper limb function ¹²¹ and the upper limb may play a minor role in controlling posture. In order for the arm to be able to move away from the body to reach a target, the body must be stable enough not to require support from the upper limb. Weakness of trunk muscles may therefore lead to the upper limb being used to support the body against gravity, and so make it unavailable for any other function.

Similarly, weak trunk muscles may make it impossible for an individual to move the body towards and object, so decreasing the functional range of reach.

Studies investigating stroke survivors' ability to reach have described multiple discrepancies from the strategies used in normal subjects. ¹²² Analyses have found that people after stroke demonstrated longer, more segmented, more variable movement and larger movement variables.¹²² Furthermore stroke survivors used compensatory trunk movements for forward transport and hand orientation¹²³.

The use of trunk restraint has been shown to result in an immediate improvement in active range of movement and co-ordination in moderate to severely affected stroke subjects⁴⁹.

1.4.10 AMOUNT OF TIME AND PRACTICE SPENT ON THE UPPER LIMB IN REHABILITATION.

In acute settings there may be a pressure for early discharge of the patient, and there is some evidence in favour of the policy of early discharge with support ¹²⁴ The role of the stroke unit therapist may therefore be to educate the patient and prevent upper limb complications rather than to provide rehabilitation to promote recovery of the limb. Therapy

often focuses on standing and walking, providing more opportunities to use the lower limbs in bilateral, weight bearing functional tasks such as walking and stair climbing, to allow safe discharge home.¹²⁵ Time for arm and hand training can be for very short periods ⁸⁷. This finding is supported by a study comparing the activities of patients in five acute stroke units, in which Berhardt et al (2007) ¹²⁶ found that in the first fourteen days after stroke only four to eleven minutes each day were spent on upper limb activities. Hammett (2010)¹²⁷ also found that therapists working in two acute stroke wards recorded spending only 10 minutes daily on UL rehabilitation.

There has been in recent years a growing number of Early Supported Discharge Teams (ESD) emerging as a means to deliver therapy post stroke. Evidence from randomised controlled trials indicates that Early Supported Discharge services can significantly reduce the length of inpatient stay ¹²⁸. However there has been variation in what defines an ESD service and the criteria for acceptance of a patient by such a team. The 2010 Care Quality Commission audit ¹³⁶ for stroke highlighted that only 18 per cent of these services have appropriate staffing. A potential issue may be that time for intensive hand and arm training may not be available with this lack of staffing. Furthermore patients who only have arm problems may miss out or be lost to the service.

An observational study in American and Canadian rehabilitation centres found that the amount of practice in post stroke rehabilitation was substantially smaller than those used in the animal studies of successful motor learning ¹²⁹. Work by Kimberly et al (2010) ¹³⁰ also investigated at the amount of repetitions patients performed in therapy sessions and found them also to be small in number in comparison to animal studies. No direct work has investigated at how much repetition of movement is needed in stroke patients to demonstrate functional improvements and evidence is unclear exactly how many repetitions are necessary for functional improvements to occur. However, the indication from research in animals and humans suggest that hundreds of repetitions are necessary in the upper limb for successful cortical reorganisation.

Stroke patients themselves report that they feel that upper limb rehabilitation and recovery is an important but neglected issue in acute stroke rehabilitation ^{131:132}. Barker and Brauer (2005)¹³² investigated the stroke survivor's perspective of upper limb recovery in a qualitative study involving interviews and focus groups with stroke survivors and their spouses. Stroke patients frequently questioned why the emphasis in acute rehabilitation

was placed on the lower limb, and walking in particular. Turton and Pomory (2002)⁸⁷ also express this view commenting that the potential for improvement may be lost due to inadequate upper limb training.

1.4.11 SUMMARY OF REASONS FOR POOR RECOVERY OF UPPER LIMB FUNCTION

As highlighted above there are a variety of factors which have been postulated to impact on upper limb recovery post stroke and may also explain the poor recovery seen. Many of these are not influenced by rehabilitation, for example the site and size of lesion are major determinants of outcome. Nevertheless, there is a belief that inadequate upper limb training may impact on the potential for recovery post stroke and that greater intensity of therapy brings about greater benefits.

The rest of this chapter will now focus on the evidence base investigating rehabilitation of the upper limb after stroke.

1.5 REHABILITATION FOR THE UL AFTER STROKE

1.5.1 REHABILITATION AFTER STROKE

Rehabilitation is defined by the WHO (2009)¹³³ as “processes intended to enable people with disabilities to reach and maintain optimal physical, sensory, intellectual, psychological and/ or social function.” Despite the successes of acute stroke management, such as thrombolysis, rehabilitation, rather than drug treatment is the main strategy for driving recovery after stroke^{134 135}. For patients, rehabilitation is fundamentally a process of relearning how to move in order to carry out their needs successfully¹³⁶.

In terms of specific rehabilitation interventions, the evidence base presents us with many gaps with only a few trials completed for any one intervention category or at different stroke delays¹³⁷. Barriers to evaluating the most effective interventions include the heterogeneity of the stroke population, the variety of stroke settings, variations in time of intervention and wide variation in outcome measures used, as well as small sample populations and methodological flaws in the published studies.

Furthermore, Wade¹³⁸ argues that rehabilitation is a 'process' involving many overlapping components and that all of these together may produce effects greater than the sum of their parts. Added to the difficulty in evaluating the most effective intervention is the impact of a patient's independent activity and the influence of family and friends.

1.5.2 CURRENT THERAPY APPROACHES

A specific therapy in rehabilitation- physiotherapy for stroke consists of a number of approaches with no conclusive evidence to support the use of one over another^{139;117}. Physiotherapy interventions following stroke have often been referred to as a 'black box'¹⁴⁰, with little available knowledge of which specific component of the intervention provided following stroke are responsible for the changes and improvements observed. (Physiotherapy techniques used for upper limb are seen in Table 1.3). This also hampers the analysis of the effectiveness of interventions when using 'conventional therapy' as a comparison/ control. The studies which are described in Chapter five and six of this thesis address the problem of the definition of treatment by making use of detailed treatment schedules, both to record experimental intervention and the conventional therapy that subjects receive (see Appendices 1 and 11)

1.5.3 CONVENTIONAL THERAPY

As mentioned above, conventional therapies (those used in routine clinical practice) used in upper limb rehabilitation following stroke use a package of different treatment activities and are difficult to describe¹⁴¹. It is known that the content of conventional therapies differs between clinical settings and over time¹⁴⁰. Traditionally the physiotherapy approach favoured in the UK has been that of neurodevelopmental physiotherapy, pioneered by Bobath, although physiotherapists report using an eclectic approach¹⁴². Two recent systematic reviews have concluded that further investigation into the efficacy of the Bobath concept is required^{143;144}; with there being ongoing debate currently regarding these conclusions.

1.5.4 REPETITIVE TASK PRACTICE

Current approaches to upper limb recovery emphasise the need for intensity and progression of treatment. Retrospective reviews of physiotherapy in stroke suggest that increased intensity is beneficial.^{145,146} Task related training, in which movement related to functional activity is directly trained has shown better results than impairment focused programs⁸⁹. In a Cochrane systematic review, French et al (2010)¹⁴⁷ conclude that task specific training can result in functional activity gain, which although modest in degree, appears to be clinically meaningful. However, the evidence for UL interventions was less clear due to insufficient good quality RCTs and difficulties in evaluating repetitive task training in clinical trials as in practice many rehabilitation interventions include complex and mixed interventions. Key elements of task specific training seem to be intensity, variability, repetition, specificity, motivation, and salience of the task to be practiced¹⁴⁸. Training should include timely and positive feedback, but all rewards should fade over time to prevent unnecessary dependency¹⁴⁹.

Table 1.3 Physiotherapy Techniques used post Stroke

Convention therapy	Sensory re-education Systematic sensory stimulation	Soft tissue mobilisation / realignment	Facilitation of muscle activity / movement	Strength training Repetitive active exercise with increasing resistance	Task specific training Active goal-directed exercise
Other techniques used for the upper limb	Balance and mobility tasks incorporating upper limb activity 	Mental imagery Cognitive practice of motor tasks	Bimanual practice Rehearsal of movements requiring the use of both arms to promote normal inter-hemispheric co-ordination	Constraint Induced Movement Therapy (CIMT) Constraint of ipsilesional arm Repetitive task specific practice with other arm	Splinting Maintenance of range of movement using external support Serial casting to improve joint range of movement
	Robotics Use of mechanical devices to guide and assist or resist practice of motor tasks	Biofeedback Provision of an auditory or visual response to a movement	Functional Electrical Stimulation (FES) Electrical stimulation of muscles to coincide with voluntary contraction	Transcutaneous Electrical Nerve Stimulation (TENS) Electrical stimulation – usually sensory	Transcranial Magnetic Stimulation (TMS) Magnetic impulse over motor cortex to stimulate muscle contraction
	Mirror therapy Use of mirror box to provide	Virtual reality Task specific	Observation to imitate Mirror motor neurons		

	an illusion of movement of the paretic limb	practice using computer generated settings	activated to stimulate areas of the CNS used when moving oneself		
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1.5.5 CONSTRAINT-INDUCED MOVEMENT THERAPY

The most promising interventions for upper-limb (arm) function seems to be constraint-induced movement therapy (CIMT), for which there has been a substantial number of trials.⁶³ In the case of CIMT, this may be due to the intensive functional retraining element rather than the constraint of the non-paretic limb ^{150 151}. There is ongoing debate about the contribution of the various elements of CIMT and studies are currently investigating the various aspects of this therapy ¹⁵². The application of CIMT is normally limited to people with some active wrist and finger extension ¹⁵³. This therapy is therefore not suitable for people with moderate to severe arm paresis. Moreover, studies also suggest that stroke survivors with severe UL paresis are frequently excluded also from task-oriented training because they have insufficient movement to actively perform a motor skill ¹⁵⁴.

1.5.6 TIMING OF THERAPY

The appropriate timing of therapeutic intervention has been debated ⁸⁷. This is due to animal studies that suggested that intensive therapy early after a lesion may be detrimental due to excessive demands made upon insufficiently recovered or oxygenated tissue ¹⁵⁵. A recent study of intensive therapy to the arm in the early stages post stroke¹⁵¹ (CIMT) also echoed those seen in the animal studies, with a worse outcome than either smaller doses of the therapy or a smaller dose of conventional therapy. However reviews suggest that more therapy is better in the acute phase ¹⁵⁶ and that potential for improvement may be lost due to inadequate training in what may be a 'critical period for recovery' ⁸⁷ in the early weeks post stroke, suggesting 4 weeks post stroke. However it should also be noted that some people may not tolerate intensive therapy in the acute phase ^{157;158}.

1.5.7 THERAPEUTIC DOSE

Dose finding is a relatively novel concept in physiotherapy research. Studies analysing therapies rarely mention how the amount of therapy provided was determined prior to the study

The absence of dose-finding studies in therapy trials may be because therapy is generally viewed to be a 'good thing' with few (if any) harmful effects.. The frequency and duration of treatment intervention in studies of therapy is often based on that used in other studies or what is practically possible in routine clinical care ¹⁰⁷. Custom and practice, whereby all patients entering a stroke unit receive 'some' physiotherapy has become established. As already noted, studies of stroke therapies suggest that more therapy in the acute stages is better ¹⁴⁶, although, in her review of the literature, Cooke (2010)¹⁵⁹ found little evidence from the published studies to support greater intensity of therapy. Unfortunately, studies do not tend to compare therapy with no treatment or a placebo, as it is considered that the recovery of patients would be disadvantaged by the absence of therapy in the acute stage after stroke ¹¹⁷. This however means that any improvements noted cannot be solely attributed to the therapeutic intervention, but may be due to other factors including spontaneous recovery ¹⁶⁰ or the attention associated with treatment. At present, clinical guidelines recommend the provision of at least 45 minutes of therapy a day⁵.

Two recent studies have evaluated dose as a precursor to randomised controlled trials comparing functional strength training and conventional physiotherapy for the lower and upper limbs.^{140;159} In respect of the upper limb, a single dose of conventional physiotherapy was surprisingly found to lead to better outcomes than a double dose of conventional physiotherapy ¹⁴⁰ The best results were obtained in the Functional Strength Training and conventional physiotherapy group, suggesting that the content of the therapy may be more important than its intensity. However, in respect of the study of lower limb therapy¹⁵⁹, no clear difference was found between Functional Strength Training and an equivalent dose of, conventional physiotherapy suggesting that in this instance intensity may be important.

Hunter et al (2011) ¹⁶¹ investigated the effect of three different doses of a sensorimotor stimulation therapy called Mobilisation and Tactile Stimulation (MTS). 76 patients were randomised into four groups-. conventional rehabilitation but no extra therapy (group one) with conventional therapy plus one of three daily doses of MTS, up to 30 (group two), 60 (group three), or 120 (group four) minutes for 14 days. The authors found that the highest doses was unable to be delivered, however a daily dose of between 37 and 66 minutes of the treatment was feasible. The study found no difference in the change in control group

compared with each of the three intervention groups. This study however is one of the first that has investigated different doses of therapy.

The need for studies that clearly specify the dose of therapy required to achieve a particular outcome is becoming more urgent in view of the increasing pressures on therapy resources (e.g. time, number of therapists, pressure to reduce patient length of stay).

Furthermore, delivering increased levels of intensity of therapy is costly and difficult to achieve in clinical practice. New and innovative ways of delivering therapy are needed to increase both intensity and total dose, in a timely manner.

1.5 ROBOTIC DEVICES IN REHABILITATION OF THE UPPER LIMB.

The use of robotics devices as an adjunct in upper limb rehabilitation has emerged as an innovative means of delivering quality therapy without increasing staffing capacity or service costs¹⁶²; in stroke survivors with varying levels of upper limb paresis, including severe paresis¹⁵⁴.

The use of robotic devices can provide high-intensity, repetitive, task-specific and interactive treatment for the impaired UL¹⁶³. This will be discussed in greater detail in Chapter 2

1.6 CONCLUSIONS

Stroke is a significant cause of disability in the population. When the arm and hand affected by stroke, functional recovery may be poor. This chapter has discussed possible reasons for why this may be the case. The site and size of lesion are major determinants of outcome which cannot be influenced by rehabilitation. Nevertheless, the use of increased intensity, with increased repetitions of movements has been seen as a way of improving arm movement and recovery. The use of rehabilitation robotics has emerged as a means to achieve these aims and this adjunct to therapy will now be discussed.

CHAPTER 2: NARRATIVE SURVEY OF THE LITERATURE INVESTIGATING ROBOTIC DEVICES AS AN ADJUNCT TO THERAPY

2.1 INTRODUCTION

Chapter One describes stroke and the impact it can have on individuals, particularly in relation to the upper limb. The previous chapter discussed the growing body of evidence which suggests that augmenting exercise therapy time early after stroke improves outcome.¹⁶⁴ This seems to be especially the case in the upper limb, where high-intensity and task-specific treatment consisting of active, highly repetitive movements has been seen to be one of the most effective approaches to recovery in arm- and hand function^{135;163;165}. Providing this augmented, high intensity therapy is labor-intensive and has resource issues. The use of robotic aids, as an adjunct to therapy, is a potential solution to the difficulties in increasing practice time. This chapter will evaluate the literature regarding this novel treatment adjunct in both subacute and chronic stroke patients. The chapter will discuss the translation of the literature and the use of robotic devices in clinical practice. Consequently, this provides an introduction and discusses the research shortfalls which are the rationale behind the studies in this thesis.

2.2 ROBOTIC DEVICES AS AN ADJUNCT TO THERAPY

Chapter One discussed the evidence supporting increased intensity of training for the upper limb which has been strongly recommended. However, delivering increased time for practice and expertise with continued specialist guidance is beyond the scope of many stroke services. The use of robotic devices has emerged as a novel and innovative adjunct to current therapy practice. Over the past ten years there has been an exponential increase in the literature investigating the use of robotic devices in the rehabilitation of arm function following stroke¹⁶²

The Encyclopedia Britannica¹⁶⁶ defines a robot as "any automatically operated machine that replaces human effort, though it may not resemble human beings in appearance or perform functions in a humanlike manner"¹⁶⁷. Robotic systems used for rehabilitation are called "cooperative" systems, as they are machines that assist in the retraining process⁹⁴. The weak arm is strapped into a hand/arm support which is connected to a robotic device.

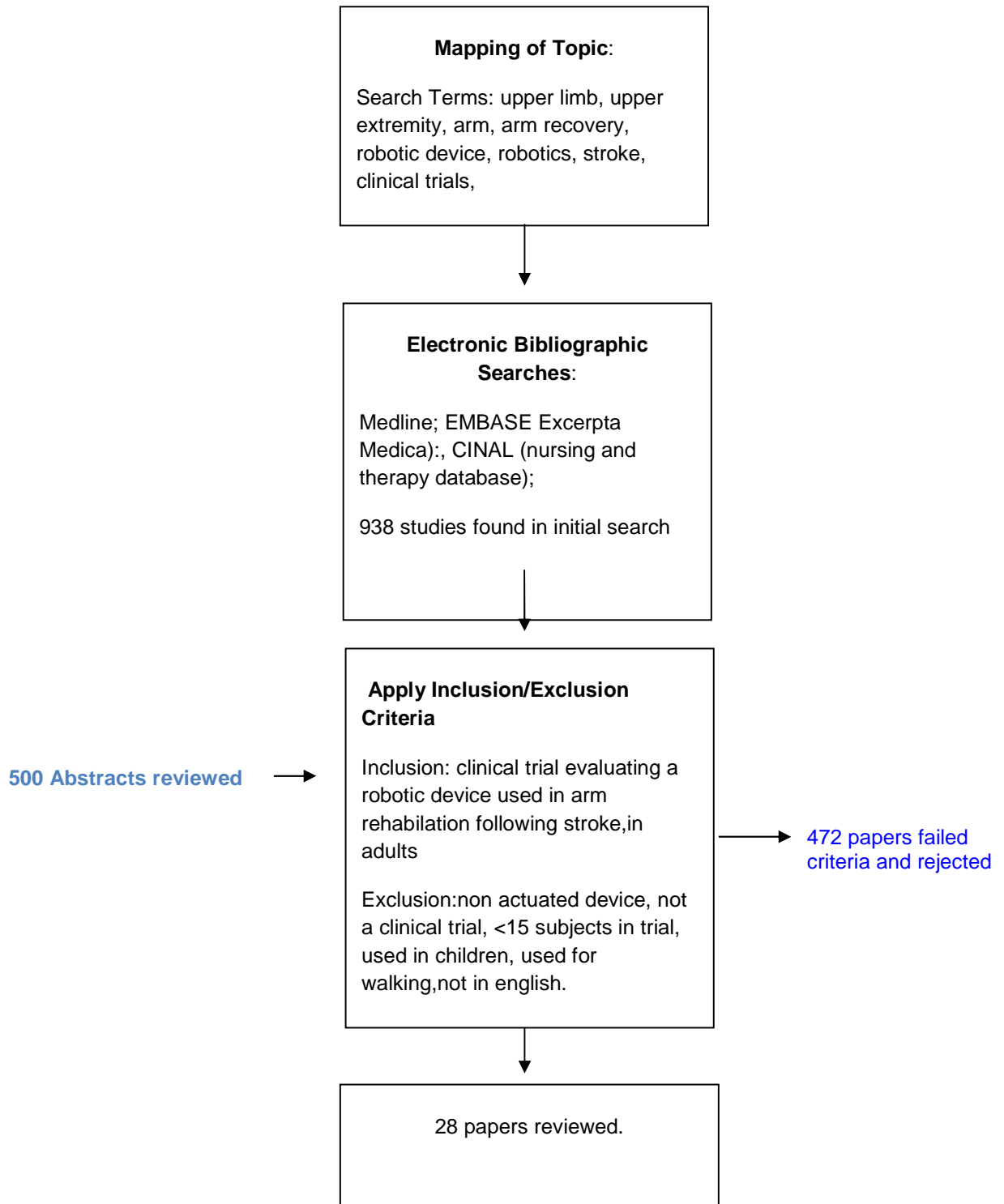
This means that the robot system can sense the movement of the user and uses that information either to passively assist, or actively resist, the patient's movements ¹⁶⁸ .

Different robotic devices target different combinations of movements, but shoulder flexion and abduction, elbow extension and wrist and finger flexion and extension are the most common movements. ¹⁶⁹ The robot is connected to a computer through which the therapist controls its actions. Instructions and visual performance feedback for the patient are provided on a computer screen. Some rehabilitation robotics incorporate computer games to help patients sustain motivation to practice for extended periods ¹⁶⁹.

2. 3 CLINICAL LITERATURE REGARDING THE USE OF ROBOTIC AIDS IN REHABILITATION.

Due to the significant body of literature that has been published regarding robotic devices, limitations have been placed on the studies which will be discussed in this literature review. Relevant literature pertinent to the thesis will only be included. This chapter will therefore only include clinical trials that have been performed examining the use of robotic devices that have an “actuator” (motor). Also only clinical trials that have recruited fifteen or more subjects will be included, and robotic devices developed and have been studied in clinical trials for arm exercise post stroke. An electronic bibliographic search was conducted in the following databases: Medline, Embase (Excerpta Medica), CINAHL, and PsycINFO. The databases were searched from 1966 to 2012. Limits were placed on each search to exclude non-English citations and nonhuman subjects using a variety of key terms, including upper limb, upper extremity, arm function, stroke, cerebral vascular accident, robotics, robotic device. A follow-up review of references was performed to find relevant articles not detected in the electronic searches. Figure 2.1 illustrates this search.

Figure 2.1: Flow diagram of systematic literature review carried out to identify literature regarding clinical trials using robotic devices.



This review found in the clinical literature the results of clinical trials (who have recruited over fifteen subjects) using five robotic systems from the USA have been published: Massachusetts Institute of Technology (MIT)-Manus; Assisted Rehabilitation and Measurement (ARM) Guide; Mirror Image Motion Enabler (MIME), pneu- WREX and HandMentor . In Europe, four systems have been developed for arm exercises post stroke, Bi-Manu-Track ; Haptic Master; Neurorehabilitation Robot (NeReBot); REHAROB . One system from Asia has been investigated in stroke patients BFIAMT . A summary of the clinical literature investigating robotic aids in upper limb rehabilitation is shown in Table 2.1

The clinical trials that have investigated the use of robotic device have all used a variety of different outcome measures to evaluate arm recovery.. Upper limb outcome measures will be discussed in detail in Chapter Four of this thesis. However, the primary outcome measure used in almost all of the studies is the Fugl Meyer upper limb score. The FMA measure consists of 33 items which are scored on a 3 point rating scale: 0=unable to perform, 1= partial ability to perform and 2= near normal ability to perform. The scores are then summed to produce a score of 66. FMA scores have been used as a means to stratify differing levels of arm impairment. However literatures vary as to scores that classify mild, moderate to severe disabilities. Daly et al^{170;171} and others^{164;172} categorise a score of <20 on the FMA as severe impairment, 20-40 as moderately impaired and >40 as mildly impaired.

2.4 STUDIES THAT HAVE INVESTIGATED THE USE OF ROBOTIC THERAPY IN THE CHRONIC PHASE OF STROKE

Most of the clinical trials focusing on robotic aids have investigated the modality in patients six months or more after stroke. These studies have found modest benefits with the use of a robotic device when compared with normal therapy. The studies carried out have been hampered by a small sample size, not all have used a control group, different durations of therapy, differing length of times using the machine, uses of a variety of outcome measures, and use of the robotic device in a mixture of settings. The trials also investigate at a variety of different robotic aids, with the majority of aids assisting with proximal shoulder and elbow movement.

2.4.1 CLINICAL TRIALS USING THE MIT-MANUS ROBOTIC DEVICE

The largest body of clinical trials investigating at robotic aids comes from the group at the Burke-Massachusetts Institute of Technology using their MIT-Manus robot and a commercial robot known as InMotion 2. This robotic arm moves a patient's shoulder and elbows either passively, actively or in a movement triggered ('active-assist') mode. The robot targets proximal arm movement and allows elbow and shoulder flexion and extension and shoulder abduction and adduction (shown in Photograph 2.1)

Photograph 2.1 InMotion2 (Interactive Motion Technologies, Inc., Cambridge, Massachusetts), a commercial version of the MIT-Manus robot.¹⁷³



Initial studies in chronic patients by this group were carried out on 20 outpatients one to five years post stroke, who received robotic therapy three times a week for six weeks¹⁷⁴. Patients in this study had moderate upper limb impairment (Mean FMA 27). The study had no control group and the patients were not given any "conventional therapy". The Modified Ashworth Scale (MAS), Fugl-Meyer test of upper-limb function (FMA), Motor Status Scale (MSS) score and Medical Research Council motor power score (MRC) were used as outcome measures, and a statistically significant improvement in these measures was seen post robotic therapy.

The same research group from Burke- Massachusetts Institute of Technology using the same program and similar patient group¹⁷⁵ , examined 42 chronic patients over six weeks, but also investigated at whether the gains from the robotic therapy remained during a four monthly follow-up. They found statistically significant gains when compared with baseline after six weeks of therapy and also after four month follow-up. Similar findings were also seen in 34 patient followed up after a four month period ¹⁷⁶. These studies are limited by their small sample size, lack of control and lack of functional outcome measures.

Finlay et al¹⁷³ have also investigated the effect of MIT-Manus robot in individuals at least six month post stroke. This study differed from the group's previous work, by looking at subjects with more severe upper limb impairment (FMA <15) and over a shorter duration (three weeks as opposed to six); fifteen subjects performed eighteen sessions with the robot. Outcome measures included the FMA, the Medical Research Council scale for muscle power (MRC), the Wolf Motor Function Test (WMFT), the Stroke Impact Scale (SIS) and robot recorded measures. Statistically significant improvement was seen in the FMA and MRC scores and the quality of movement. The choice of outcome measures in this paper seems to be inappropriate. The authors state clearly that the main reason for carrying out this study was to address the role of robotic device in subjects with severe upper limb impairment, however they then chose an outcome measure (WMFT) that was devised and used specifically in constraint induced therapy studies, where typically impairment is mild.

The MIT-Manus study group have also investigated the impact of their robotic aid with half the duration and twice the intensity¹⁷⁷ and also looked at the specific exercises the robot training provides¹⁷⁸. In both studies all subjects improved with robotic therapy and there seemed to be no difference in outcome depending on the type of exercise performed by the robot, suggesting that increased intensity has the potential to shorten the duration of rehabilitation.

These studies are of interest as they suggest that the use of a robotic device can assist in reducing impairment six month or more post stroke. However as the treatment was not compared against a control group, and, or therapy it is impossible to know whether it is specifically the robotic device that is useful or that the subjects improved because they were having a form of "therapy"/repetitive practice. Furthermore, only two of the studies

Ferraro et al¹⁷⁶ and Finlay et al¹⁷³ study examined the functional impact of the device and no patient reported measures were recorded.

Some attempt to address the limitations of their previous work has been undertaken by the Burke Institute group by performing a small randomised control trial on a group of 22 outpatients six month or more post stroke¹⁷⁹. Subjects (eleven in each arm) either used a robotic arm three times a week or were treated by a therapist for sessions matched both in duration and number. Outcome measures were the FMA, MRC, MAS, SIS and Action Research Arm Test (ARAT). Improvements in the FMA and MRC were seen after six weeks of treatment, with no significant change between robotic therapy and therapeutic input. No change was seen with the ARAT or SIS. Improvements in the impairment measures remained three month post treatment. Such a finding suggests that therapy in some form remains beneficial in the chronic stage post stroke. This study is again limited by its small sample size, and absence of specific arm patient reported measures.

Subsequent research by the MIT-Manus group includes a hand/wrist component to the robot to allow a “whole arm” device¹⁷⁴. This is an important addition to the robot as the previous model only trained proximal movements and results in the groups studies have seen only proximal improvements in the FMA^{180,176,181}. Krebs et al¹⁷⁴ piloted the whole-arm device in 47 chronic stroke subjects, using a pretest-post test comparison. The subjects received (as in previous studies by this group) robotic therapy three times a week for six weeks. The FMA was used as the outcome measure and significant improvements were seen post treatment.

The “whole arm” device has been investigated in a multicentered Randomised Control Trial (RCT) involving 127 chronic stroke patients¹⁷¹. This is the largest study currently to have been performed looking at the use of a robotic device. Patients in this study were randomized into one of three groups: one group used the robot for a twelve week period (the patients in this group carried out three weeks of performing shoulder and elbow movements with the robot, three weeks of shoulder and grasp movements and three weeks of wrist movement), one group received one hour therapy for twelve weeks, one group received their “usual care”- (i.e no additional therapy)¹⁷¹. The primary outcome for the study was a change in the FMA at twelve weeks. The mean scores in this measure were found to be better in the robot group than the “usual care” group, but worse than that for the group receiving therapy. No statistical significance was found between groups.

However, at 36 weeks a significant difference was found between the robot group as compared with the usual care” group, but not with intensive therapy.

The findings from Lo et al (2010) ¹⁷¹ study supports the premise that increased intensity of therapy can assist in improving upper limb movement. However, the study does not differentiate that the use of a robotic device is any better than increased therapy. The study had a predominance of men, and a lack of blinding in study-group assignments. The study also involved a selected group of veteran stroke patients visiting selected medical centers and this may not be able to be generalized to the wider stroke population.

2.4.2 CLINICAL TRIALS USING THE MIME ROBOTIC DEVICE

Another key group looking at robot-assisted therapy for the arm after stroke, use the Mirror Image Movement Enabler device (MIME) ¹⁸². This is a proximal arm device that allows reaching with shoulder flexion, abduction, adduction, external rotation, elbow extension and flexion. The device has a bimanual mode, in which it moves the impaired arm to the mirror image position of the unimpaired limb (shown in Photograph 2.2).

The device has been looked at in a randomized control trial of 27 chronic stroke subjects who received 24 one hour sessions over two months) ¹⁷² The robot group practiced shoulder and elbow movements assisted by the machine. The control group received conventional therapy and five minutes use of the robot at each treatment session. The FMA, Functional Independence Measure (FIM) and biomechanical measures of strength and kinematics were measured. The study found that the robot group had statistically larger improvements in the FMA. The group also had larger gains in strength and reach. At six monthly follow-up there was no statistically significant differences in the two groups, although the robot group demonstrated a non statistical improvement in the self care and transfer section of the FIM.

The research group do detail which therapy was given in the “conventional therapy” arm of the study, although how much of the time in the therapy session the subjects practiced upper limb movement is unclear. As Kahn(2006) ¹⁸³ comments the findings of this trial rather than indicating the benefits of robot therapy, may instead be an indictment of convention therapy which may not have maximized movement practice. However, this is the first study that suggests that the use of additional upper limb practice by use of a robotic device improves upper limb recovery more than therapy alone in chronic subjects.

Photograph 2.2 MIME robotic device¹⁸²



2.4.3 CLINICAL TRIALS USING THE ARM ROBOTIC DEVICE

The Arm Robotic device (Assisted Rehabilitation and Measurement Guide- ARM) is a linear device allowing reaching in a straight line (elbow and shoulder flexion, elbow extension). Kahn et al (2006)¹⁸³ looked at training reach using the device in ten chronic stroke subjects; they also used nine matched control subjects who practiced reach without the robotic device. Each subject trained for twenty four, forty five minute sessions over eight weeks. Although both groups showed improvements in The Raicho Los Amigos Functional Test of the Hemiparetic Upper Extremity, there was no significant difference between groups. This is a similar finding to the MIT-Manus group RCT¹⁷¹ but differs from the MIME trial ¹⁶⁵. The authors suggest possible explanations for this discrepancy, the movements of the robots are different, intensity of use varied and the MIME allows a bimanual mode of training. However, these may have also been due to the small sample number, and differing outcome measures, so no conclusive reason for the difference can be drawn.

2.4.4 CLINICAL TRIALS USING THE HAPTIC MASTER ROBOTIC SYSTEM

This robotic device was designed by Fokker Control Systems, following an European Union project entitled GENTLE/s. The robot system is a haptic interface arm which de-weights the arm, allowing shoulder and elbow flexion, extension, elbow pronation and supination, wrist flexion and extension. Two studies have been reported using this system, using a single case study design on 20 and 31 chronic stroke subjects^{108;184}. The subjects in randomized treatment phases used the robotic system (phase B) and sling-suspension (phase C). Each phase lasted for three weeks and subjects had 30 minutes of intervention three times per week. The range of active shoulder flexion, FMA and MAS were measured each visit. Both studies found that each subject had a varied response to the measurement and intervention phases; however trends suggested that the rate of recovery was greater during the robot-mediated therapy phase.

These studies^{108;184} suggest trends towards improvement with robotic therapy, but no statistical significance was found and the data was found to be highly variable. Coote et al(2008)¹⁰⁸ also comment that the results of their study and previous studies using the Haptic Master may have been hampered by the small amount of robot therapy the subjects received during the research trials.

Photograph 2.3 Haptic master robotic device



2.4.5 CLINICAL TRIALS USING THE BI-MANU-TRACT ROBOTIC SYSTEM

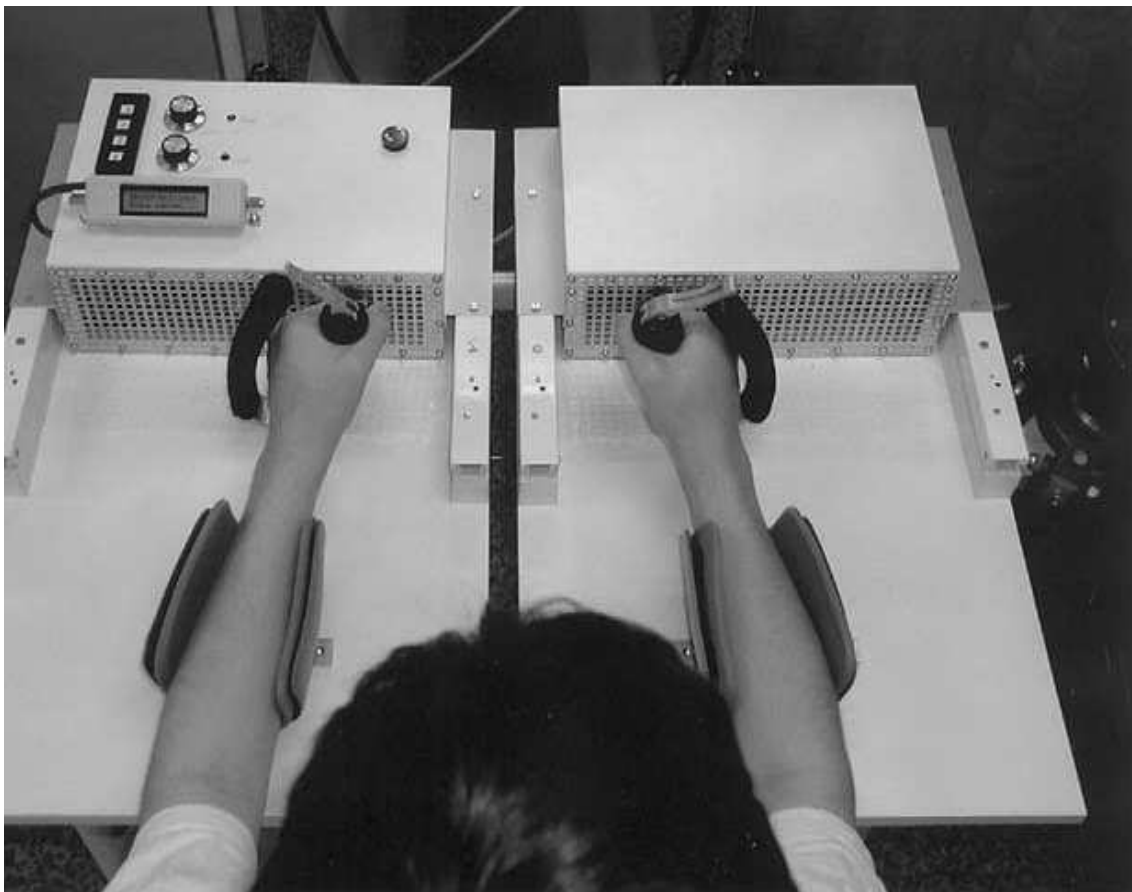
Bi-Manu-Tract is a robotic system which allows training of forearm pro-/supination and wrist flexion/extension and training is done bimanually¹⁸⁵. A pilot pre-post test trial of the device in twelve chronic stroke subjects has been performed¹⁸⁵. Each subject used the robot for fifteen minutes five days a week for three weeks. The patients were all undergoing rehabilitation programs of 45 minute daily physiotherapy and occupational therapy in addition to the use of the robot system. Subjects were followed-up at three months. The MAS and arm section of the Rivermead Motor Assessment Score were used as outcome measures. A significant reduction in MAS was seen with robot therapy but no meaningful change in the Rivermead Score was demonstrated. These effects did not continue at three months. There are a number of limitations with this study: its lack of control; small sample size; and small duration of time subjects used the robot.

Liao et al (2011)¹⁸⁶ investigated the use of Bi-Manu –tract in ten participants who were more than six months after a stroke, compared to ten control subjects. Participants used the device for 90 minutes, five days a week for a four week period. The control group

received therapy that was designed to be dose-matched with the intervention group. A statistically significant improvement was seen in the FMA measure with use of the robot in comparison to the control group. This study used accelerometers as a means to record subjects arm movements during the trial. The results of the study found that the group who used the robot appeared to incorporate their affected arm more in daily tasks than the control group. Furthermore, a significant difference was also seen in a patient reported outcome measure (ABILHAND). This is one of the few robotics studies that have found functional improvements with use of a robotic device. Liao et al (2011)¹⁸⁶ acknowledge that this finding may be due to the participants in the robotic intervention also performing 15-20 minutes of “functional activity training”. No follow-up analysis at a different time period was conducted on the participations, so longer term benefits of the intervention is unclear.

The same study group ¹⁸⁷ have also published a pilot RCT on 18 chronic stroke subjects (mean 21 months post stroke) with moderate to mild upper limb impairments (mean FMA of 37 to 44). Participants were randomized into three groups: high intensity use of the Bi-Manu-tract (high repetitions of movements), low intensity use of the device (lower repetitions of movements), or conventional therapy for 90 or so minutes, five days a week for four weeks. The primary outcome measure was the FMA. Analysis revealed that the higher intensity group showed significantly better improvements in FMA than the lower intensity group. The study did not measure the intensity of the conventional therapy group, so matched comparisons of intensity of treatment between the groups cannot be ascertained. In addition, although this small study randomized subjects, the higher intensity group had higher baseline FMA and MRC scores, which may have biased the outcomes.

Photograph 2.4 Bi-Manu-Tract



2.4.6 CLINICAL TRIALS USING THE BFIAMT SYSTEM.

Chang et al (2007) ¹⁸⁸ report on the bilateral force-induced isokinetic arm movement trainer (BFIAMT). This device assists with bilateral push and pull movements to simulate sanding activity, which the authors describe as a popular therapeutic activity in early rehabilitation ¹⁸⁸. They looked at using the BFIAMT in 20 subjects at least six months post stroke. Each subject performed a training program consisting of 30 minutes using the robot, ten minutes of conventional therapy for three sessions a week over eight weeks. The FMA was used as the primary outcome. A statistical significance was found in the FMA and in terms of grip, push and pull strength following use of the aid. This study had no control group; furthermore subjects had conventional therapy at the same time as using the robot device so it is difficult to distinguish which caused the beneficial effect. In addition, the studies assumption that sanding activity is a common place therapy activity may be true in Taiwan but this has not been seen to be the case in other countries, such as the UK¹⁸⁹ .

2.4.7 PNEU-WREX

The Pneu-WREX is a robotic device which was based on another non –actuated device which has been studied in clinical trials called WREX¹⁹⁰ . It allows elbow flexion/ extension, shoulder horizontal abduction/adduction, shoulder flexion/extension, and shoulder forward backward translation. The device incorporates a passive weight support mechanism, the device can provide assistance as needed for a patients to actively participate and be able to complete 3D tasks. Grasp and release hand movements are also incorporated. The robot has been trialed in a pilot randomized control trial of 27 subjects (thirteen subjects used the robot, fourteen controls).¹⁹⁰ Subjects at least six months post stroke, who had a mean FMA score of 23, were seen for one hour sessions three times a week for eight to nine weeks. Subjects either performed a set of exercises (control group) or used the device. A statistical significance was seen in FMA scores in the robot group compared to the control group. This was not seen on three month follow up and nor was this seen in other more functional outcome measures such as the MAL.

2.5 TO SUMMARIZE THE LITERATURE LOOKING AT ROBOTIC AIDS IN CHRONIC STROKE SUBJECTS.

This literature review highlights that there is a growing body of literature investigating the use of a variety of robotic arms in chronic stroke patients. The majority of these studies have shown improvements in upper limb impairments with this therapy, but have been hampered by small sample size, lack of control, no conformity in duration and intensity of use of the device or outcome measures. Trials have rarely used functional outcome measures or patient reported measure. It is encouraging however that the studies have suggested improvement in this chronic group, where recovery is seen to be slower and has plateaued¹⁹¹. The most beneficial time to introduce robotic therapy also needs evaluating, and it could be proposed that more benefit may be seen with this therapy in the acute/subacute stages post stroke. This may be because as Lum et al (2006) ¹⁹² postulate the central nervous system may be more “plastic” in the acute phase. Furthermore, the use of robotic therapy may assist in the prevention of secondary maladaptive changes related to increased passive tissue stiffness and contracture.⁶²

2.6 STUDIES THAT HAVE LOOKED AT ROBOTIC THERAPY IN ACUTE/SUB ACUTE PHASE POST STROKE.

This review will now discuss the recent research trials that have investigated the use of robotic devices in acute/subacute stroke population.

2.6.1 CLINICAL TRIALS USING THE MIT-MANUS DEVICE.

The MIT-Manus group initially began looking at their robotic aid in acute subjects. They have published results on 96 patients ^{181;193-196}. All subjects were randomly assigned to a robot treatment or control group and were within three weeks of their first stroke with upper limb weakness and undergoing rehabilitation as inpatients. Subjects spend 45 minutes using the robot, five days a week for four weeks. Control patients used the robot without the motor on with them using their unaffected limb to move the affected arm one or two hours a week. A statistical significant improvement was found in motor power (MRC scale) and MSS for the elbow and the shoulder in the robot group compared with the control group. The FIM was found to significantly improve in the robot group for 56 patients¹⁸¹ but when extended to 96 patients this significance was not seen¹⁹⁷.

These findings again point to the benefit of robotic use, and contrast to the group's findings in chronic subject which did not specifically find a beneficial advantage of the device when compared to "convention therapy"¹⁷⁹. There may be a number of reasons for these differing results: a) the stage post stroke (acute/subacute stage may pragmatically be a better time to use this therapy); b) larger sample size; c) more intensive use of the robot (daily as opposed to three times a week); d) subjects were inpatients undergoing rehabilitation so potentially more motivated to use this device as a therapy adjunct. These factors however, mean that direct comparison between the groups work in chronic compared to acute stroke population, cannot be made.

It is unclear in the research discussed above, what inpatient rehabilitation the subjects were having, consisted of, and the therapy that both groups received were not defined in the literature. This is disappointing, as the findings of this body of work rather than being indicative of the benefits of robot therapy may instead be a reflection of convention therapy which may not have maximized movement practice ¹⁸³. Furthermore the study did not compare the use of the robotic device to equal amounts of conventional therapy, leaving the question whether it was the additional therapy that was beneficial or the use of the robotic device.

Rabadi et al (2008)¹⁹⁸ have also looked at using the MIT-Manus in a preliminary randomized control in acute stroke. Patients who had had single incident stroke within four weeks of admission to an inpatient rehabilitation facility were included in the study. Thirty subjects were enrolled and randomized into either a standardized therapy group, use of an arm ergometer or use of the MIT-Manus robotic device. All patients received standard, inpatient, post stroke rehabilitation training for three hours a day, plus additional 40 minutes session of the activity-based therapy. In total subjects were seen for twelve sessions. Primary outcome measures were the FMA, Motor Status Score, and FIM.

The study found a similar degree of improvement in the discharge scores in all of the outcome measures. This suggested no difference between the three types of arm therapy with all three resulting in a decrease of impairment. The study had several limitations: It used a small sample size which may have precluded detecting important differences between groups; secondly the study used shorter, less intensive arm therapy sessions than other studies that have shown improvement in motor scores with robotic therapy^{181;193-}

¹⁹⁶.

2.6.2 CLINICAL TRIALS USING THE MIME DEVICE.

The MIME group¹⁹² have also looked at the device in subacute subjects, one to five months post stroke. Thirty subjects were randomly assigned to either control or three different robot group (unilateral/bilateral/combined). All patients received fifteen one-hour treatment sessions over a four week period. The FMA , MSS, FIM and muscle power were used as outcome measures. Statically significant improvements in FMA were seen post robotic therapy than in the control group. However, as in their previous study in chronic subjects, gains were equivalent at the six month follow- up. When looking at improvements in individual subjects, robotic therapy was seen to be most effective in subjects in a middle range of motor impairments (falling between fifteen and 23 inclusive on the proximal FMA). This result is very much in keeping with the groups work in chronic strokes and adds strength to support of the use of the device. Caveats remain such as the small sample size and choice of outcome measures.

Burger et al (2011)¹⁹⁹ conducted a randomized control trial comparing the use of the MIME robotic device for two different dose intensities (low dose of fifteen hours or high dose of 30 hours) with an additional fifteen hours of conventional therapy (in addition to usual care). Subjects (n=54) in this study were subacute strokes (seven to 21 days post stroke). As opposed to the groups previous studies in chronic patients, gains in the primary outcome measure (FMA) was not significantly different between the groups. This may be explained by small number of subjects in each treatment group. Another possible explanation is that the study matched treatment intensity of use of the robot and conventional therapy. This leads to the question is it the robotic device or just additional therapy that results in achievement of reported gains?

2.6.3 CLINICAL TRIALS USING THE BI-MANU-TRACK SYSTEM.

Hesse et al¹⁸⁵ using their Bi-Manu-Track, extended their previous work in chronic stroke patients to look at 44 patients, four to eight weeks after stroke. Subjects were randomly assigned to either using the robotic device or using electrical stimulation. All participants practiced 20 minutes every workday for six weeks. The robot group performed 800 wrist

movement repetitions per session with the robot, while the patients using electrical stimulation performed 60 to 80 wrist extensions per session. The FMA was used as the primary outcome measure, and was found to improve in both groups but significantly more in the robot group. This was also seen in muscle power. On three month follow-up this improvement remained.

This study also found that both proximal and distal arm control improved in the robot group. Hesse et al¹⁸⁵ recommend from this finding that emphasis of treatment should shift from the shoulder to the forearm, hand and fingers. Although this is a notable recommendation, the evidence from their small, feasibility RCT is not strong enough to currently generalise. Furthermore, the findings of the study must be treated with caution as using electrical stimulation as a control treatment may be standard treatment in Germany; however this is not the case in the U.K, where guidelines by the Royal College of Physician (2012)⁴ advice that FES should not be used as a stand alone treatment due to the lack of evidence currently supporting this modalities use.

2.6.4 CLINICAL TRIALS USING THE REHAROB THERAPEUTIC SYSTEM

The Robotic rehabilitation system for upper limb motion therapy for the disabled (REHAROB Therapeutic System) is a system that allows shoulder and elbow movements in a constant velocity. A trial of the system on thirty subjects has been performed using a mixed subject population consisting of stroke and head injury patients.²⁰⁰ Subjects in the study randomly assigned to either robotic therapy or control therapy. Every subject received 30 minutes of therapy on 20 consecutive work days; the robot group also received additional 30 minutes using the robot. A battery of outcome measures was used, including the FMA, Rivermead, FIM and MAS. The subjects improved in all measures post treatment. The MAS for shoulder adductors and elbow flexors showed a statistically significant change only in the robot group.

The authors²⁰⁰ report that one of the stated aims of their study was to see the effect of tone of using the robot, and interesting this is the only measure that showed a significant change from the control group. (with a reduction in Ashworth scores in shoulder flexion and elbow flexion tone following use of the robotic device). This finding is difficult to

interpret and compare with other studies using different devices and the study uses subjects with different diagnosis and different stages in their recovery.

2.6.5 CLINICAL TRIALS USING THE NE-RE-BOT DEVICE

Masiero et al (2007)²⁰¹ have looked at robotic therapy in acute stroke patients using a novel robotic device the Neuro-Rehabilitation Robot (NeReBot). This device performs flexion, extension, pronation and supination, adduction and abduction of shoulder and elbow. It can be used in supine as well as in sitting.

In a study investigating the effectiveness of this robot, 35 single incident acute strokes, a week post stroke, were randomized to either robot group or control group ²⁰¹. All subjects received daily therapy and the experimental group received additional robotic training consisting of two sessions a day, four hours a week for five weeks. The control group used the robot except that the exercises were performed with the unimpaired limb. Blinded outcome measures were taken at baseline, five weeks, three month and eight month follow-up. The study used the FMA, MRC scale, FIM, Trunk Control Test (TCT) and MAS. Compared with the control group, the robot group showed significant gains in muscle power, FMA for the proximal arm and the FIM. These gains were sustained at three and eight month follow-up. The authors do not clarify why the control group used the robot with their unaffected arm and this requires further explanation.

The same study group updated this study in 2011²⁰² performing a further trial in 21 subjects (patients were within 20 days post stroke). This study compared conventional therapy (40 minutes of treatment to the proximal arm in addition to patients normal inpatient therapy), with use of the NeReBot for two 20 minute training session (these patients also received their usual inpatient therapy). Both groups improved in outcomes (these included the FMA, muscle strength as measured by MRC and Motor-FIM), no statistical difference was found between the groups. This study does not discuss how subjects were randomized into the groups, used small sample size and used no specific upper limb functional outcome measures.

2.6.6 CLINICAL TRIALS USING THE HAND MENTOR DEVICE

This device uses a pneumatic artificial muscle (actuator) and provides biofeedback regarding muscle activation and control.²⁰³ The device focuses on wrist movements. Activation of the air muscle rotates a bar about a pivot point positioned in line with the axis of rotation about the wrist. This action extends the wrist and fingers. The device has EMG biofeedback. It has been looked at in a RCT comparing use of the device and Repetitive Task Practice (RTP) against just RTP.²⁰⁴ Seventeen subacute subjects participated, seven in the control group and ten in the active group. Subjects completed three weeks of five days a week therapy, with the control group practicing four hrs of RTP. The other group performed two hours with the device and two hours RTP. The Stroke Impact Score was used as an outcome measure. Both groups reported significant improvement in hand function with the intervention and this was also seen on follow-up.

2.7 SUMMARY OF RESEARCH TRIALS THAT HAVE LOOKED AT ROBOTIC THERAPY IN ACUTE/SUBACUTE STROKES.

This literature discussed above suggests that robotic therapy may be a useful adjunct to assist in upper limb recovery and that it may allow greater improvement in this as compared with “conventional therapy” when used in acute or the sub acute stroke population (with more studies suggesting this than seen in the chronic population). There has however been a paucity of research trials that have looked at robotic therapy in the acute stroke population. Theoretically, the acute phase post stroke is when potential for significant functional gain is greater. Therefore further research looking at robotic devices in the early stages post stroke is needed. The studies in this theses aim to fill this research gap.

Four systematic reviews of robotic therapy (including a recently updated Cochrane review) have been carried out to date^{163,205,206;207} . These reviews have summarized that this therapy adjunct may improve impaired motor function and strength in the paretic arm but currently there is no evidence to suggest they improve functional abilities. They conclude that the results of studies looking into this therapy must be interpreted with caution because there were variations between the trials in the duration, amount of training and type of treatment and in the patient characteristics.

There has been little conclusive evidence from the findings of the literature as to whether improvements seen with the use of robotic devices are due to the device itself or via simply delivering more opportunity for UL practice. Recent work by Liao et al (2011)¹⁸⁶ comparing dose-matched control and robotic therapy found significant improvements in the robotic group, suggesting a specific effect of the robot itself. However further clinical trials to investigate matched control and robotic therapy are needed.

2.8 OTHER FACTORS

There is a growing body of literature suggesting that stroke rehabilitation may improve functional performance for some patients⁸⁹. There is however, little information available about what constitutes optimum treatment, skill level and experience of therapists providing treatment¹⁸⁹. Furthermore, progress in stroke rehabilitation is impeded by insufficient detail about components of treatment and description of convention therapy activities²⁰⁸. This lack of detail and description of what consists therapy, limits replication of research studies and the incorporation of research findings into clinical practice¹¹⁷. Robotic therapy provides standardization of therapy and quantification of rehabilitation, which has been a problem dogging conventional therapy trials²⁰⁹.

2.9. UNRESOLVED ISSUES WITH THE USE OF ROBOTIC DEVICES

2.9.1 FACTORS AFFECTING THE TRANSLATION OF ROBOTICS INTO CLINICAL PRACTICE

Despite the emergence of the myriad of robotic device listed above (with many more developed that have not yet, been clinical tested), there has been little translation of robotics currently into clinical practice. The current evidence does not illustrate that any particular robotic system is of any added benefit over another. For robotic aids to be effective, their design and protocols for use must be driven by clinical need and developed as a result of engagement with all interested parties; engineers, therapists, patients and their careers²¹⁰. There are currently unanswered questions regarding the involvement of

robotic systems within the rehabilitation process. This is also the case regarding how practical it is to use robotic systems in clinical practice. The research in this thesis aims to address some of these issues and the remainder of this chapter will outline important unresolved issues and gaps in the current literature. These will be highlighted in each section.

2.9.2 WHAT PLACE DO ROBOTIC SYSTEMS HAVE WITHIN THE REHABILITATION PROCESS?

For robotics to be used as an adjunct to therapy, they need to be able to deliver increased intensity of practice, increased accuracy of performance and engage patients in the therapeutic process. Do we have any current evidence that suggests robotic systems are able to achieve these needs?

2.9.3 WHO WOULD BENEFIT FROM USING A ROBOTIC DEVICE?

In patients with severe upper limb paresis the ability to participate in repetitive task – orientated activities is limited because they have insufficient underlying movement²¹¹. Barker et al ¹³² found that stroke survivors felt that “not enough movement to work with” was the greatest barrier to recovery. This may explain why stroke patients with severe paresis show limited improvement ^{212,125} Robotic devices may be a means for these patients to perform repetitive, task-specific activity. The literature reviewed here has found improvements in subjects with “severe arm paresis” (defined as a FMA <15)¹⁹². Many of the robotic devices use an “active-assist” mode where the robot can assist movement. However some trials found that the greatest improvement seen with using robotics seems to occur in subjects with FMA greater than 20 on admission to trials ¹⁰⁸. Furthermore there is discrepancy in the literature as to what FMA score is defined as “severe”. ¹⁰⁸ An added complication to this is that current outcome scales may not be capturing changes in function which may be of relevance to patients. Hayward et al (2010)¹⁵⁴ in a systematic review of interventions to promote arm recovery in stroke survivors with severe paresis found that robotics hold some promise, however the effectiveness will be dependent on whether they lead to improvements in the ability to perform everyday tasks.

One of the aims of the studies detailed in this PhD is to evaluate if people with stroke with little arm movements can use the device. Furthermore does the level of arm paresis impact on functional recovery.

2.9.3 INTENSITY OF PRACTICE

In the acute setting, studies have found that stroke patients spend little time performing upper limb activities¹⁷. Pilot studies suggest that an advantage of robotics devices is that they enable increased practice intensity and repetition of arm movements, compared with conventional therapy²⁰⁶. As yet, clinical studies of conventional treatment regimes have not established optimum treatment intensity although a growing consensus is that it could be as much treatment as is tolerated. For many patients after stroke, this may be as little as 20 – 40 minutes treatment a day. *It is currently unknown the proportion of patients following stroke who would be able to use a robotic device, and would benefit from using such a device.* This would be extremely useful clinical data, and would facilitate the integration of the use of these devices into routine clinical practice. The studies discussed in this thesis will perform exploratory work to look at this area.

Clinical trials using robotic devices have varied the amount of treatment provided, ranging from 30 minutes^{181;193;194} to 90 minutes each work day¹⁷⁶. This amount of variation makes analysis of the benefits and outcomes of different devices difficult. Studies that have tried to match the intensity of robotic therapy to the number of movements generated during conventional therapy did not find any significant benefit of one technique over the other¹⁸³. In light of these equivocal results, *future trials comparing the efficiency of robotics to standard therapeutic practice need to incorporate clear descriptions of the comparator treatment to establish that robotic training doses actually increase movement repetitions.* Although recent publications^{186;187} have begun to explore this, further investigation in this is required and this will be explored in this thesis.

2.9.4 INCREASED ACCURACY OF PERFORMANCE

The complexity of sensory and motor integration needed for dexterity and functional use of the arm complicates the rehabilitation process (as discussed in Chapter One). Evidence from neuroimaging suggests that functional recovery from stroke is influenced by task-specific training or everyday use of the arm and hand.^{46;109;213} Most devices focus on shoulder and elbow movements, rather than wrist and hand movement. In contrast, most functional tasks demand co-ordinated proximal and distal movements in order to reach, grasp and manipulate an object.

Many of the robotic systems described previously are aimed primarily at training reaching movements, and have shown improvements proximally and at an impairment level. Few studies showed functional change with use of a robotic device.²⁰⁵ It is difficult to conclude the precise reasons for this. Has there been a lack of translation from improvements at an impairment level to activities of daily living due to patients practicing proximal movements with the robotic systems rather than distal movements? The Lieu et al (2012)¹⁸⁶ study is one of the few studies that has shown some functional improvements with the use of a robotic device (the Bi-manu-tract which trains wrist and hand function,) so this would concur with this premise. *Or is it because many trials used impairment measures rather than measures looking at function?* Again the Liao et al (2012)¹⁸⁶ study is one of the few studies that have used activity and participation outcome measures to look at functional gains with the use of a robotic device. There is however, currently no single reliable and valid tool that captures the complete range of arm function in stroke patients²¹⁴. (This area will be discussed in greater depth in Chapter Four.) Furthermore there is a debate in neuro rehabilitation about the role of impairment level interventions versus functional training²¹⁵.

The studies in this thesis will use impairment and activities and participation measures to address this question.

2.9.5 ENGAGING PATIENTS IN THERAPY

Robotic aids are designed specifically to enhance the motivation and adherence of patients to treatments. In particular, having control over the difficulty level of the motor task, gaining feedback on performance, practising a meaningful movement, providing a suitable challenge and ensuring successful task-completion even with minimal active movement can influence patient motivation and produce different behaviours²¹⁶

.Furthermore, the competitive scoring system of feedback offered by robotics provides a gratifying incentive to enhance enjoyment and motivate patients to complete tasks and reach certain goals²¹⁷.

However, a potential problem with robotic aids is that reduced therapist-patient interaction may negatively affect motivation .²¹⁶. The therapeutic relationship and rapport between the therapist and patient can influence patients' intrinsic motivation and make exercising more effective ^{216, 218;219}. If the interaction between the patient and the clinician is an important determinant of adherence then use of a robot may actually reduce adherence ²²⁰ .

Empirical research is required to explore this range of factors impacting on the motivation of stroke patients to engage with use of robotic devices, to advance research in the field of rehabilitation robotics. This is again an area which will be examined in the studies detailed in this thesis.

2.10 POTENTIAL DIFFICULTIES WITH THE USE OF ROBOTIC DEVICES IN CLINICAL PRACTICE

In addition to these issues surrounding what a robotic system might do within the rehabilitation process, there are also practical implications of the use of robotic devices in clinical practice.

2.10.1 IS THERE A RISK WITH THE USE OF ROBOTICS?

Current robotics literature suggests that dropout rates from studies were very low and adverse reactions were rare²⁰⁵. In commercially available robotic devices, the machines have had to be extensively tested and pass very tough certification processes. Devices also have redundant safety measures. However, for robotic machines to be of clinical use they must be reliable and safe for use by patients with or without therapists, with mechanisms in place to ensure that if breakdown occurs it is without risk.

Few studies discuss shoulder pain with regard to use of robotics, and this has not been systematically explored in the literature. This is interesting considering the high rate of reported shoulder pain post stroke^{72;221} ⁷⁰and observations that early-onset pain hinders

the motor recovery of the upper limb and may hamper daily activities²²² (Discussed in Chapter One Section 1.5.8). *Systematic reporting of adverse events and a thorough review of the incidence of shoulder pain with the use of robotic devices would be helpful.* This is included in the studies described in this thesis.

2.10.2 HOW DO PATIENTS AND THERAPISTS RESPOND TO ROBOTIC THERAPY?

Despite, the growing body of literature describing new robotic devices, there are surprisingly few papers that have addressed patients and therapists views of using robotic devices. This is despite the growing recognition that, if medical devices are to be of real value, then the needs and capabilities of the users must be considered ²²³ . Table 2.3 summarises the literature that has investigated this.

Krebs et al(1998)¹⁹⁵ in their initial clinical trial of the Mit Manus system report the responses of 20 participants to five questions. Burger (2000)¹⁸²also described user involvement into the development of the MIME system. Coote and Stokes (2003) ²²⁴ used a questionnaire survey to ascertain eight patients with stroke and six therapists' perceptions of the Haptic Master Robotic system. A questionnaire was used to gather information about patient's satisfaction with the Reo Therapy System²²⁵ (a robotic device). All of these found positive responses to the robotic systems.

Five further studies identified that robotics are acceptable to patients ^{134;162;216;226;227} and two have found that therapists had positive attitudes to robotic devices^{162,226} (Table 2.2 describes these studies in more detail). Limitations with these studies are: a lack of clarity on question development; questionnaires were often administered by treating therapists, use small sample sizes, the psychometric properties of the questionnaires are not established, and questions or statements used are not always published. *Further rigorous qualitative data on users' perceptions on systems is needed to provide greater depth to the current work.* This will be discussed further in Chapter Seven of this thesis.

2.10.3 IS IT COST EFFECTIVE TO USE A ROBOTIC DEVICE?

The cost effectiveness of robotic devices has yet to be probably evaluated. Many of the devices are expensive and storage and placement of the device in ward based rehabilitation settings can be an issue.²²⁸ Lo et al^{171;229} have looked at a cost analysis in their RCT which compared the Mit Manus system to matched intensive therapy and usual care. They found that the average cost of delivering both intensive comparison therapy and robotic therapy was more expensive than normal care. The cost of both intensive therapy and the use of the device were comparable, this questions previous opinion regarding using robotic systems as a means to deliver cheaper intensive upper limb therapy. A potential application of robotic systems is that they could be used as a means of independent repetitive practice for the patient, further work looking at cheap devices that can be used independently needs to be performed.²²⁸ .

Two recent papers have tried to address this issue, by looking at the use of non actuated (no motor) arm orthoses^{212;230} These devices are smaller, more portable machines. Housman et al.(2009)²³⁰ describing the advantages of using cheaper non-assisted devices, commented that it has not yet been demonstrated that the expensive actuator components of the robot devices are necessary for the therapeutic effects associated with robotic therapy. Clinical trials using these devices have also found improvements in impairments^{212;2304}. They do not, however, provide clear evidence that non-assisted devices work as well as robotic devices with actuators, nor that they are more cost effective or practical to use at the bedside or in the patient's home. Furthermore, a non-robotic device cannot provide active-assisted movement which limit the use of the device to mild to moderate impaired stroke survivors (although Barker et al (2008)²¹² used the SMART Arm in severely impaired subjects), nor can it record or adjust programs as required with treatment progress.

This area of cost effectiveness is a key area for future research in robotic and the comparison between robotic and non robotic aids needs to be established in larger studies. *The level of supervision and assistance required to use robotic aids needs to be considered in the cost-benefit analysis.* Preliminary work in this area will be examined in this thesis.

2.10.4 ROBOTIC THERAPY TO REPLACE THERAPIST IN UPPER LIMB REHABILITATION?

Interestingly, the few studies that have looked at therapy perceptions of robotic devices^{134;162;231} have found that therapists do not report feeling threatened by the emergence of robotic technology. The current generation of robotic devices support this assumption, as none have the capability to reproduce the hands-on facilitation of muscle activation provided by a therapist. Engineers are now working towards programming robotic devices to specifically simulate therapeutic input with replicable visual, auditory and/ or sensory feedback²³², to emulate as closely as possible the interaction between the patient and the human therapist²³².

Therapists have suggested that a robotic device used for therapy should be versatile enough to be able to train many degrees of freedom and ranges of motion and to provide therapy from standing, sitting and lying positions²³¹. This is not possible with any of the existing robotic systems²³². Technological advances have developed significantly in the last 10 years, but as yet small, cheap, versatile robots that can be used in the patients' home environment or at the bedside have not yet been used in clinical trials.

2.11 CONCLUSION

The use of robotic device in upper limb rehabilitation is a new development to support recovery of arm function following stroke. Robotic devices may be a means for stroke patients to perform repetitive, task-specific activity leading to improvements in function.^{89;233} A variety of different robotic devices have been trialed in clinical studies, most of these assist with proximal arm movements, but devices which assist with distal activity have also been developed.

This review has detailed the current evidence base for robotic devices as an adjunct to therapy for the upper limb. The clinical trials which have been described in this chapter have found modest benefits with the use of a robotic device when compared with normal therapy. The studies carried out have been hampered by a small sample size, not all have used a control group, different durations of therapy, differing length of times using the

machine, uses of a variety of outcome measures, and use of the robotic device in a mixture of settings. The trials also look at a variety of different robotic aids.

Current literature does not provide clear evidence of either increased intensity or better functional outcomes, but there is enough evidence to pursue this approach.

Improvements in design both of the robots and the clinical trials used to evaluate them are needed.

Unanswered questions remain from the literature, with further work needed to investigate:

- a) The use of robotic devices in the acute stage when potential recovery is the greatest
- b) The functional benefits of robotic devices
- c) Patients perceptions of the devices
- d) Risks with the devices
- e) What proportion of acute stroke patients could potentially benefit from using a robotic aid? No current work has looked into this area which has important clinical information
- f) Can patients with differing levels of arm paresis use the device?
- g) What resources are required in terms of trained and untrained staff?
- h) Does the use of different upper limb outcome measures that look at patient function better reveal any activity and participation benefit with robotic devices?

The studies described in this thesis hope to address these questions through a mixed methodological approach. Chapter Three will now detail the aims and objectives of these studies. Particular emphasis will be given to conducting studies that explore the translation of robotics from experimental research into clinical practice. Five stages will be used to this achieve these aims (as detailed in Chapter Three) and will be discussed in the next chapters.

Table 2.1: Summary of Clinical Trials that have looked at Robotic Therapy in Stroke Patients.

Author	Robot Type	Movements performed by robot	Stage post stroke	Sample size	Method used in trial	Intervention			Outcome measure	Results
						Duration	Frequency	Minutes/session		
Aisen et al (1997) ¹⁹³	MIT-Manus	Planar reaching movements	Acute , 3 weeks post stroke	20	RCT	6-7 weeks	Daily	1 hour	FMA, FIM, MSS	Statistical significance in MSS in robotic group
Volpe et al (2000) ¹⁸¹	MIT-Manus	Planar reaching movements	Acute , 3 weeks post stroke	56	RCT	5 weeks	Daily	1 hour	FMA, MP, MSS, FIM	Improvements seen in motor performance in shoulder and elbow in robotic group
Fasoli et al (2004) ²³⁴	In- motion 2	Planar reaching movements	Chronic	42	Pre-post test	6 weeks	3 times a week	1 hour	FMA, MRC, MSS, MAS, pain shoulder. 4 month f/u	Sig FMA, MSS, MRC. And on f/u with the robot
Daly et al (2005) ¹⁷⁰	MIT-Manus	Planar reaching movements	Chronic	12	RCT, FES control group	12 weeks	5 days a week	1 hour	ARAT, FMA	Sig. in ARAT in robotic group

Author	Robot Type	Movements performed by robot	Stage post stroke	Sample size	Method used in trial	Intervention			Outcome measure	Results
						Duration	Frequency	Minutes/session		
Ferraro et al (2003) ¹⁷⁶	MIT-Manus	Planar reaching movements	Chronic	34	pre-post test,	18 sessions,	3 times a week	1 hour	FMA, MP, MSS, FIM, MAS	Stat sig FMA and MP and FIM UL in robotic gp
Stein et al (2004) ¹⁷⁸	In-motion2	Planar reaching movements	Chronic	47	Pre- post test	6 weeks	3 times a week	1 hour	FMA, MAS, MSS, MRC	Improvement in FMA, and force measurements
MacClellan et al (2005) ¹⁷⁷	In motion 2	Planar reaching movements	Chronic	27	Pre and post test	3 weeks	2 sessions a day, 3 days a week	1 hour	FMA, MSS, WMFT, motor power	Significant improvements in all measures
Finley et al (2005) ¹⁷³	In motion 2	Planar reaching movements	Chronic	15	Pre and post test	3 weeks	2 sessions a day, 3 days a week	1 hour	FMA, MSS, WMFT, MP, SIS	Improvements in FMA and MP
Krebs et al (2008) ¹⁷⁴	In motion 2	Planar reaching movements, hand/arm component	Chronic	47	Pre and post test	6 weeks	3 days a week	1 hour	FMA	Improvements in FMA

Author	Robot Type	Movements performed by robot	Stage post stroke	Sample size	Method used in trial	Intervention			Outcome measure	Results
						Duration	Frequency	Minutes/session		
Lo et al (2010) ¹⁷¹	Mit Manus "Whole Arm device"	Able to perform both planar reaching and hand grasp movements	Chronic	127	RCT	12 weeks	36 sessions	1 hour	FMA, WMF, SIS	Statistical significance in FMA when compared to usual care but not intensive therapy
Lum et al (2002) ¹⁶⁵	MIME	4 modes of movement/bilateral	Chronic	27	RCT 6 month f/u	2 months	24 sessions	1 hour	FMA, BI, FIM. Strength, reach	Statistical significance in FMA
Lum et al (2006) ¹⁷²	MIME	4 modes of movement-and bilateral	Subacute	30	RCT	4 week	15 sessions.	1 hour	FMS, MSS, FIM, MAS, motor power	Stat Sig in proximal FM scores with robot, but gains equivalent 6 month follow-up. Less benefit from bilateral mode.

Author	Robot Type	Movements performed by robot	Stage post stroke	Sample size	Method used in trial	Intervention			Outcome measure	Results
						Duration	Frequency	Minutes/session		
Burger et al (2011) ¹⁹⁹	MIME	4 modes of movement- and bilateral	Acute	54	RCT	4 weeks	15 sessions	Low dose- 15 hours High dose- 30 hours	FMS, MSS, FIM, MAS, motor power	No sig seen in the groups
Amirabdollahian et al (2007) ¹⁸⁴	Haptic-Master	Shoulder movements	Chronic	31	RCT, (Cross-over). Robot V sling suspension	9 weeks	Three times a week	30 minutes.	FMA, MAS goniometry	Multiple regression model, positive but modest trends favoring both interventions
Coote et al (2008) ¹⁰⁸	Haptic-Master	Shoulder movements	Variety, sub-acute, chronic		RCT, (Cross-over). Robot V sling suspension	9 weeks	Three times a week	30 minutes.	FMA, MAS goniometry	Multiple regression model, positive but modest trends favoring both interventions

Author	Robot Type	Movements performed by robot	Stage post stroke	Sample size	Method used in trial	Intervention			Outcome measure	Results
						Duration	Frequency	Minutes/session		
Liao et al (2011) ¹⁸⁶	Bi-manu-Tract	Mirror sup/wrist flexion	Chronic	20	RCT	4 week	5 days a week	90 minutes	FMA, accelerometers, ABILHAND	Stat sig in robotic group in all measures
Hsieh et al (2011) ¹⁸⁷	Bi-manu-Tract	Mirror sup/wrist flexion	Chronic	18	RCT	4 week	5 days a week	90 minutes	FMA, MRC	No stat sig seen
Hesse et al (2005) ¹⁸⁵	Bi-Manu-Tract	Mirror sup/wrist flexion	Sub acute	44	RCT	6 weeks		20 minutes	FMA, MRC, MAS,	FMA scored improved in both.
Chang et al (2007) ¹⁸⁸	BFIAMT	Allows push and pull movements	Chronic	20	pre and post test	8 weeks		10 min of normal therapy, 30 min of robot	FMA, MAS, Frenchay arm test	No stat sig in any measures. Grip and reach improved
Fazekas et al (2007) ²⁰⁰	REHAROB	Shoulder and elbow movements	Range (1-87) months post lesion	8 TBA/22 stroke	RCT	20 days		30 minutes	FMA, MAS, ROM, RMA, FIM	Stat sig FMA, range elbow, RMA, FIM self care

Author	Robot Type	Movements performed by robot	Stage post stroke	Sample size	Method used in trial	Intervention			Outcome measure	Results
						Duration	Frequency	Minutes/session		
Masiero et al (2007) ²⁰¹	NeReBot (direct-drive wire actuation)	Shoulder and elbow (3 degree of freedom)	Acute	35	RCT (8 month follow up)	5 weeks	Twice a day	4 hours a week	MRC, FMA, FIM, TCT, MAS, VAS (tolerance)	Stat Sig seen in MRC, FIM, FMA with robotics. Sustained on follow-up 3/8 months
Bovolenta et al (2009) ^{235, 42}	Reo Therapy System	Forearm movement	Chronic	14	Pre and post test	4 weeks	5 days a week	45 minutes	FMA, MAS, Ashworth, VAS (pain and tx stratification), FAT, B&B, FIM, ABILHAND, TUG, EQOL	Significance seen in FMA, B&B, FAT and FIM
Treger et al (2008) ⁴³	Reo Therapy System	Forearm movement	Sub-acute	10,	pre and post test	3 weeks	5 days a week	45 minutes	Questionnaire, FMA, Manual Functional Test	Stat Sig seen in FMA

Author	Robot Type	Movements performed by robot	Stage post stroke	Sample size	Method used in trial	Intervention			Outcome measure	Results
						Duration	Frequency	Minutes/session		
Casadio et al (2009) ⁴⁴	Braccio di Ferro	Planar device, shoulder and elbow movement	Chronic	10	Pre and post test	10 weeks	Once a week	60 and 75 minutes	FMA, MAS, Ashworth	Significance seen in FMA,
Takahashi et al (2008) ⁴¹	HWARD	pneumatically actuated hand device grasp and release movements.	Chronic	13	Pre and post test	3 weeks	15 sessions over weekdays	1.5 hours	ARAT, box and Block, FMA, NIH, GDS, NSA, SIS, Ashworth, goniometry	Stat Sig seen in FMA and ARAT. fMRI also used in study
Reinkensmeyer et al (2012) ¹⁹⁰	Pneu - WREX	Shoulder movements, release and grasp hand	Chronic	27	RCT	9 weeks	3 times a week	60 minutes	FMA, MAL, RLAFT	Stat Sig seen in FMA
Kahn et al (2006) ¹⁸³	ARM	Linear shoulder and elbow	Chronic	19	RCT	8 weeks	24 sessions	45 minutes	RLAFT	No significance seen

Author	Robot Type	Movements performed by robot	Stage post stroke	Sample size	Method used in trial	Intervention			Outcome measure	Results
						Duration	Frequency	Minutes/session		
Kutner et al (2010) ²⁰⁴	Hand Mentor	Wrist and finger extensor/flexion.	Sub acute	17	RCT	3 weeks	5 days a week	2 hours robot, 2 RTP. Control 4 hours RTP.	SIS	Stat significance seen in both groups. Single questions in SIS improved more in robot group/

NB: * Finlay et al (2005) and Cootes et al (2008) describe preliminary data from larger studies which are reported in other studies.

Abbreviations: Rx: Treatment, Stat Sig: Statistical significance, RCT: Randomized Control Trial, CV: Cardio vascular.

SOMC: Short Orientation Memory Concentration assessment, RLAFT: Ranchos Los Amigos Functional Test, GDS-Geriatric Depression Scale, NSA-Nottingham Sensory Assessment, FMA: Fugl Meyer Assessment (UL section); FIM: Functional Independence Measure; TCT: Trunk Control Test; MAS: Modified Ashworth Assessment; VAS: Visual Analogue Scale, MAS: Motor Assessment Score; RMA: Rivermead Motor Assessment Score. MSS: Motor Status Score, WMFT: Wolf Motor Function Score, MRC: Medical Research Council Muscle Power Score, MAL: Motor Activity Log, SIS: Stroke Impact Scale, RTP: Repetitive task Practice

Table 2.2: Details of Studies reporting Patient and Therapists Opinions of Robotic Therapy.

Study Name	No. of patients	No. of therapists	Robotic Device	Question Format	Questionnaire Reproduced	Results
Dijkers et al (1991) ⁶⁵	22	11 OTs	Unnamed	Closed Yes/No Questions	Yes	Device to be safe, enjoyable and helpful
Krebs et al (1998) ⁶⁴	10	-	MIT-Manus	Likert Scale Statements	Yes	Device comfortable, and wanted to perform more therapy on it. Patients did not wish to replace therapist-led rehabilitation with just use of the robot.
Coote & Stokes (2003) ³²	8	6PTs	Haptic Master	Likert Scale Statements and Closed Yes/No questions	Yes	Both patients and therapists showed a positive disposition to the device. Therapists were concerned about shoulder placement, patients were not.
Holt et al (2007) ⁶³	6	4 OTs 4PTs	IPAM	Likert Scale Statements	No	robot comfortable and safe

Study Name	No. of patients	No. of therapists	Robotic Device	Question Format	Questionnaire Reproduced	Results
Doornebosch et al (2007) ⁶⁶	10	10	ACRE 2	Unknown	No	Patients and therapist were satisfied with the device. Therapists were concerned about the arm support.
Treger et al (2008) ⁴³	10	-	Reo™	Likert Scale Statements	No	Positive patient response
Lee et al (2005) ⁷⁰	17	17	Robotic devices in general	Unknown	No	Therapists responded positively to the idea of a robotic device in a clinical setting.
Hughes et al (2011) ⁶⁷	5	-	Unnamed	Likert Scale Statements and open question	Yes	Device well accepted and tolerated by patients
Lu et al (2011) ²³⁶	-	233	Robotic devices in general	Online survey	Yes	Top attributes of a device included: facilitating a number of arm movements, can be used in sitting, having virtual activities specific to daily living, being useful in-home and having resistance adjustable to client needs. Also, the device should be low cost.

CHAPTER 3. PURPOSE OF THESIS

3.1 INTRODUCTION

This PhD builds on the current literature (described in Chapter Two) on the use of robotic devices as an adjunct to upper limb rehabilitation, with the aim of addressing some of the unanswered questions regarding the use of this invention. Particular emphasis will be given in this thesis to conducting studies that explore the translation of robotics from experimental research into use in clinical practice.

Unanswered questions that this thesis will explore are (also mentioned in Chapter Two):

1. A systematic review of upper limb outcome measures
2. What proportion of acute stroke patients could potentially benefit from using a robotic aid?
3. Is there a difference in the potential benefit of the aid depending on the severity of arm paresis?
4. Can patients with differing levels of arm ability use the robotic device?
5. What intensity of practice can the device provide and is this beneficial?
6. Do patients find the device acceptable and feasible to use?
7. Are there any risks with the use of a robotic device?
8. What resources are required in terms of trained and untrained staff? Is the use of a device clinically feasible in a hospital setting?
9. Does the use of different upper limb outcome measures that look at patient function better reveal any activity and participation benefit with robotic devices?

3.2 THE RELATIONSHIP BETWEEN THE INDIVIDUAL STUDIES AND THE OVERALL INVESTIGATION

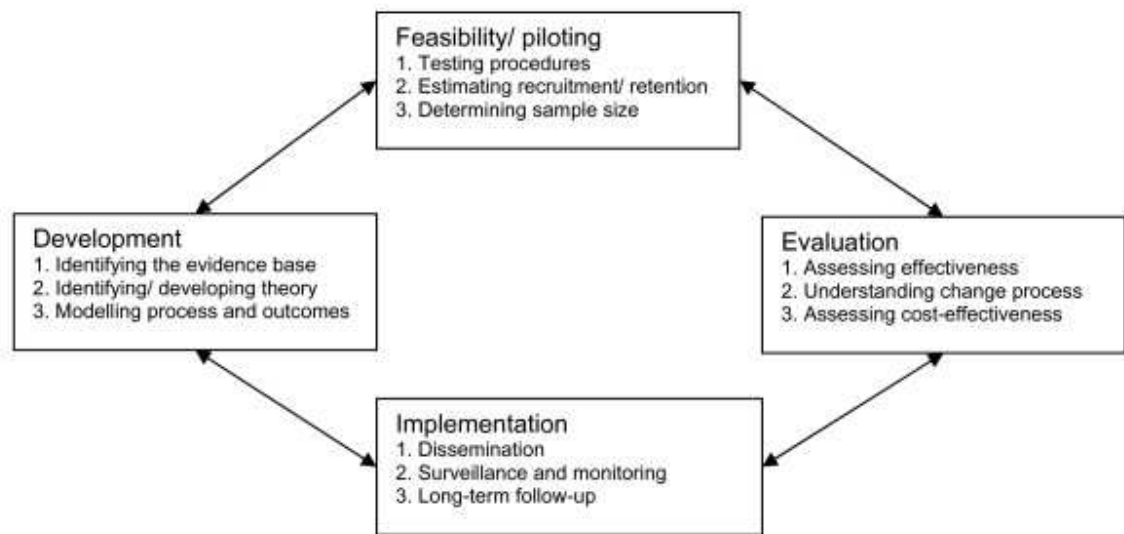
The overall investigation described in this thesis combines a number of methodological approaches and phases of investigation. The studies comply with the strategy set out in the MRC guidance for the development and evaluation of complex interventions^{237;238}.

Neurological rehabilitation may be conceptualised as a complex intervention. Complex interventions are built up from a number of components, which may act both independently and inter-dependently e.g. behaviours, parameters of behaviours (e.g. timing, frequency) and methods of organising those behaviours (e.g. type of practitioner, setting, location). Evaluating such interventions is challenging²³⁸. The MRC published 'A framework for development and evaluation of RCTs for complex interventions to improve health' in 2000²³⁷ and revised this in 2008²³⁸. The work described in this thesis followed the approach defined in the framework, uses a combination of both quantitative and qualitative methodology. This mixed methods research approach combines elements from both qualitative and quantitative paradigms to produce converging findings in the context of research questions²³⁹.

3.3 THE MEDICAL RESEARCH COUNCIL FRAMEWORK

The framework was designed to facilitate good research practice and to provide investigators with guidance in recognising the unique challenges which arise in the evaluation of complex interventions. The framework recognises the iterative approach needed for this type of research. The framework describes four separate stages²³⁷: The guidance recognises that a linear model of successive phases may not be appropriate to the development of complex interventions. The framework identifies key elements in the development and implementation process and these are shown in Figure 3.1 below.

Figure 3.1 MRC Framework²³⁸



Each stage of the framework will now be discussed and how these relate to the studies in this thesis:

3.3.1 STAGE ONE: DEVELOPMENT

The framework discusses that it is important to establish a theoretical basis that suggests the intervention may have an expected effect. A number of approaches are used to develop the theory that underpins the subsequent development of a complex intervention. These include an analysis of individual experience, consensus views and a review of relevant literature. The literature review is an important part of any study; completed at the start of a study to help with deciding a topic; reviewing the published and unpublished literature it is often returned to throughout the study with the original search being expanded on²⁴⁰. An iterative process is often used to develop the search terms²⁴¹ and used in the Cochrane review processes; the aim being to develop a search that is as inclusive as possible and therefore yield the most papers. After each search the terms are revised and the searches re-run. It is also important to establish the outcomes that are aimed for²³⁷.

With this in mind two comprehensive systematic reviews were carried out to firstly identify research which has looked at the clinical use of robotic devices in upper limb rehabilitation and the outcome measures used to evaluate the intervention. These reviews are found in Chapters Two and Four.

3.3.2 STAGE TWO: FEASIBILITY AND PILOTING

This stage includes testing procedures for their acceptability, estimating the likely rates of recruitment and retention of subjects, and the calculation of appropriate sample sizes²³⁸ Exploratory trials allows the effects of an intervention to be seen and measured and uncover where weaknesses in the study design exist. The framework comments that a mixture of qualitative and quantitative methods may be needed, for example to understand barriers to participation and to estimate response.

From the review carried out in Chapter Two, unanswered questions were identified in the robotic literature (which has been stated in section 3.1). These questions raised the need for further feasibility and piloting work to be carried out before definitive evaluations (Stage three of the framework could be carried out). This consisted of five components:

1. A systematic literature review was carried out to establish the most reliable, valid and responsive available limb outcome scales to use in the following trials; (Chapter Four)
2. An evaluation of consecutive acute stroke patients established the proportion of acute stroke patients that potentially benefited from rehabilitation using a robotic device (recruitment study, a phase II exploratory trial); (Chapter Five)
3. A exploratory randomized controlled trial determined how the use of a robotic device (ReachMAN) can be delivered in practice and provided estimates of the sample size needed for a definitive study (a phase II, exploratory trial); (Chapter Six)
4. A qualitative study was completed to investigate patients perceptions of the robotic device. (Chapter Seven)

5. A psychometric analysis used new & traditional methods was carried out to evaluate and select the most appropriate outcome measures for future trials (Chapter Eight)

Each chapter will discuss separately the reasons behind the methodology chosen to evaluate the different components of the questions.

3.3.3 STAGE THREE EVALUATING A COMPLEX INTERVENTION

The MRC framework discusses that there are many study designs to choose from, with different designs suiting different questions. The gold standard is a definitive RCT which in the earlier version of the MRC framework²³⁷ was described in phase iii as ‘to compare a fully defined intervention to an appropriate alternative using a protocol that is theoretically defensible, reproducible and adequately controlled, in a study with appropriate statistical power’²³⁷.

Quantitative research describes the accurate assessment of the outcome or effects of an intervention that necessitates the careful manipulation of that intervention (experimental variable), in controlled conditions, and a comparison of the group receiving the intervention with an equivalent control group. It is essential that systematic errors (bias) and random errors (chance) are minimized. This requirement necessitates carefully designed, rigorously carried out studies, using reliable and valid methods of measurement, and with sufficiently large samples of participants who are representative of the target population²⁴².

One of the aims of study performed in Chapter Six was to provide estimates of the sample size needed for a definitive study i.e. to be able to progress to this stage of the framework.

3.3.4 STAGE FOUR IMPLEMENTATION

This last stage of the framework discusses getting evidence into practice. This was one of the key drivers for the research studies described in this thesis. Chapter Two highlighted the gap between the current research and the clinical use of robotics in upper limb rehabilitation. These gaps formed the background to the work performed and this area will be further discussed throughout the thesis.

3.4 ReachMAN Robotic Device

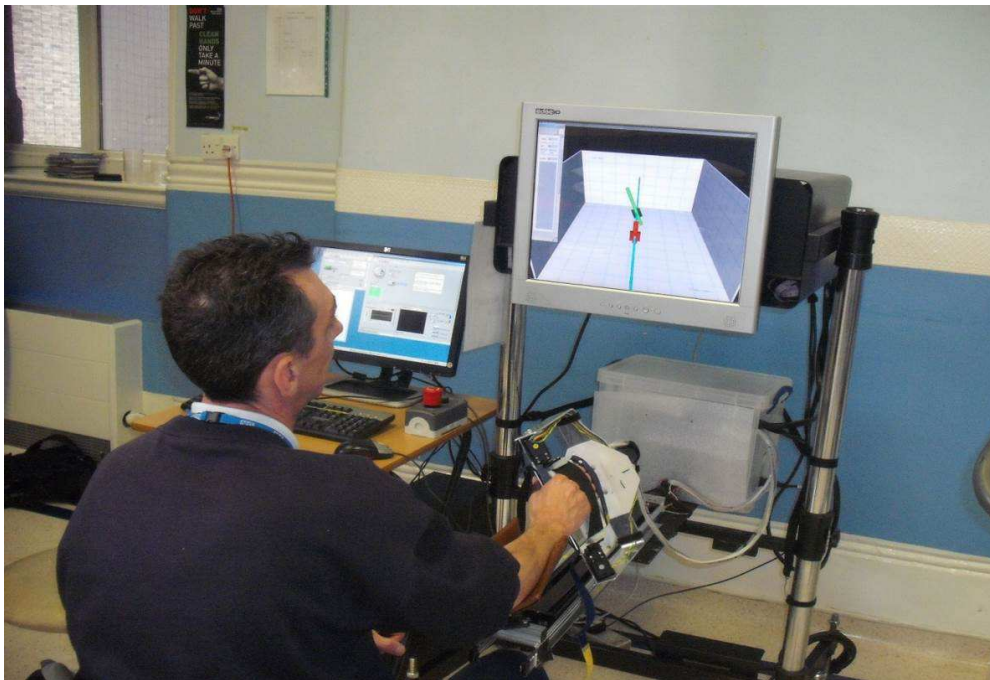
ReachMAN is a robotic device that was developed by a group of engineers at Imperial University in conjunction with the author of this PhD, Dr Diane Playford and Consultant physiotherapist Ann Holland. Burdett and colleagues aim to develop small, low cost and portable robotic aid designed for use at a patient's bedside in a rehabilitation unit or at home ²⁴³. ReachMAN (Figure 3.2) facilitates shoulder flexion/extension, wrist pronation/supination and finger flexion/extension. These movements are fundamental components of many common everyday tasks such as opening a door, using a key or switching on an oven. ReachMAN is set up as a multilevel game with each level placing a greater demand on the patient.

The device is capable of continuously assessing the patient's motor performance recording speed, direction & strength of voluntary activity and duration of time & intensity of practice. The height of the ReachMAN is adjustable for standing or seating position. The subject's arm is rested on the arm support to prevent excessive use of the shoulder. Subjects train with ReachMAN while holding to the robot handle (secured with Velcro band) and looking at the computer monitor which provides visual feedback. The visual feedback displays the movement of the robot handle relative to the target position.

All exercises are performed as a similar task where subject have to move the handle to a target position within 10 seconds and hold at the target for about 0.5 seconds. A new target appears when the subject has successfully completed a trial. If the time limit is breached, the trial is considered a fail, and the robot would help complete the movement to the target, after which a new target would appear.

ReachMan was piloted on three subjects prior to the machine use in the studies. This pilot is described in Yeong et al (2010)²⁴⁴.

Figure 3.2. ReachMAN Robotic Device



3.4 HYPOTHESIS

The premise on which the use of the robotic device (ReachMAN) was based on was that recovery of movement and function of the hand and arm would be promoted by providing intensive, repetition of movement to the contralesional upper limb after acute/ subacute stroke. This had been tested via the null hypothesis that the use of a ReachMAN make no significant difference to the recovery of the hand and arm after stroke. The alternative hypothesis that ReachMAN would significantly improve recovery of the upper limb in acute, sub-acute stroke was proposed.

3.5 AIMS OF THE DIFFERENT STUDIES

- The aims of the review of upper limb outcome measures:
 - a) Make recommendations about choice of outcome measure for RCT
 - b) Assess feasibility and acceptability of range of measures

- c) Evaluate psychometric properties
- The aims of the recruitment study were to:
 - a) Determine future recruitment criteria
 - b) Determine the rate and timing of recruitment in practice
 - c) Make recommendations about choice of outcome measure for RCT
- The aim of the exploratory randomized control study was to determine how the intervention would be delivered in clinical practice to:
 - a) Establish positioning and set-up needs of a range of patients so that they can interface with the device, and how long this takes
 - b) Establish frequency and duration of device use in practice
 - c) Define any training needs for physiotherapists and therapy assistants
 - d) Evaluate the effects of the use of ReachMAN in an acute/ sub-acute stroke population
 - e) Provide sample required for a definite RCT
- The aims of the qualitative study was to:
 - a) Explore patients' and carers' perceptions of using ReachMAN
 - b) Inform future robotic design and treatment protocols.

3.6 SUMMARY

This Chapter has identified the research questions and aims for this thesis. The following chapters describe the original work that was carried out to explore these aims and unresolved issues in the robotic literature.

CHAPTER 4:A SYSTEMATIC REVIEW OF UPPER LIMB OUTCOME MEASURES

Work described in this chapter has been previously published:

Baker K, Cano SJ, Playford ED. Outcome measurement in stroke: a scale selection strategy. *Stroke* 2011; 42(6):1787-1794.

4.1 INTRODUCTION

Chapter One and Two highlighted that upper limb recovery following stroke poses particular challenges. Recent innovations in treatment such as repetitive practice through the use of robotics hold promise for improving upper limb recovery. Chapter Two identified that the current research looking at the use of robotics in upper limbs have found little improvement in function with the use of these devices. Is this due to the intervention or could a factor be the outcome measures that have been used to assess this? Evaluating the impact of a novel treatment such as the use of robotics in upper limb rehabilitation increasingly depends on the use of valid, reliable, and responsive outcome measures. The aim of this chapter is to describe a systematic review that was carried out to identify the most appropriate outcome measures for use in the trials described in Chapter Five and Six.

4.2 BACKGROUND

There has been an increasing awareness over recent years over the importance of the selection of rating scales used in studies. In fact, the conclusions made from neurologic studies are dependent on the rating scales used, and these conclusions in turn influence patient care, prescribing, policy making, and the expenditure of public funds²⁴⁵. The adequacy of these choices depends directly on the scientific quality of the rating scales. In acknowledgment of this fact, there has been a rapid increase in the application of rating scale science (known as psychometrics) in health outcomes measurement in neuroscience.

To assist with the growth of psychometrics and the increased use of rating scales, a number of guidelines have been published for the use of scales in clinical trials: In 2002 the Scientific Advisory Committee of the Medical Outcome Trust (MOT) produced guidelines for the development and validation of patient reported outcome questionnaires²⁴⁶; The US Food and Drug Administration (FDA)²⁴⁷ have also recently published draft guidelines for rating scales in clinical trials which have been described in the Lancet²⁴⁸. The MOT and FDA documents are detailed and outline a wide range of

issues relating to the development and validation of Patient Reported Outcome Measures (PROM), based on current widely used psychometric methodology. Although these detailed guidelines refer to PROM they can be applied to all rating scales.

4.2.1 PATIENT REPORTED OUTCOME MEASURES (PROM)

To evaluate an intervention, data collection is required pre and post intervention. Historically outcomes were traditionally measured with clinician rated outcomes e.g. FMA which is a method of clinicians quantifying upper limb movement. However, this type of outcome misses a large aspect of change which the patient experiences. It is these experiences from the patient's perspective, which bring a wider understanding of the impact of an intervention or treatment. Prompted by the need for evidence based health care there has been a transition from these clinician rated outcomes to a more holistic approach that encompasses a wider range of health variables²⁴⁹. Researchers have increasingly turned to developing measures that capture this broader concept of health including psychological well-being and satisfaction with treatment. These outcomes are generically called patient reported outcome measures (PROMS).

PROMS are described as a measurement of any aspect of a patient's health status that come directly from the patient (i.e. without the interpretation of the patient's responses by a physician or anyone else)²⁵⁰. A PROM can be used to measure the impact of an intervention on one or more aspects of a patients' health status, ranging from purely symptomatic (e.g. response of a headache) to more complex concepts (e.g. ability to carry out activities of daily living) to extremely complex concepts such as quality of life. Data generated can provide evidence of a treatment benefit from the patient's perspective. For this data to be meaningful, however, there should be evidence that the PROM effectively measures the particular concept that is studied²⁵⁰.

There are advantages with PROMS. These are:

- Some treatment effects are only known to the patient;
- There is a desire to know the patients perspective about the effectiveness of the treatment; and
- Systematic assessment of the patient's perspective may provide valuable information that can be lost when filtered through a clinician's evaluation.

Disadvantages: PROM require the respondents to be literate and cognitively intact to a level where they can respond to closed questions with a choice of set responses. Pre-coded response choices may not be sufficiently comprehensive, and not all answers may be easily accommodated. Some respondents therefore maybe 'forced' to choose inappropriate responses²⁴⁰.

The use of patient reported outcome measures in stroke research is a relatively new development²⁵¹ and is complicated in this population by cognition and communication difficulties which can occur in stroke survivors²⁵². Dorman et al (1999)²⁵³ for example asked 2253 stroke patients to complete EuroQol and SF36 via mail and found that 50% of the stroke subjects were unable to complete the questionnaires by themselves. Absent data can cause biased estimates of stroke treatment effect, lessen the power of a study to detect responsiveness and reduce the generalisability of the results in. The inclusion of proxy data can assist in improving the above problems, although the use of proxy respondents should be approached with caution^{254;255}.

Typically in upper limb measures PROM will look at functional activities that may involve the whole arm. Clinician rated measures are more likely to examine impairment level movement or focus on a single task performed at varying degrees of difficulty. Both have their place but for interventions to be successful they must make a difference to patients' lives and this can only be successfully captured in a patient reported outcome. Therefore despite the problems described above with the use of PROM in the stroke population, it was felt to be important to use both clinician rated and PROM in the studies described in this thesis.

4.2.2 CHOOSING UPPER LIMB OUTCOME MEASURES AND SCALES FOR THE STUDIES

Various reviews have looked at upper limb outcome measures in both stroke and hand and arm function tests in other upper limb disorders^{254;256;257}. The most recent review has been carried out by Ashford et al (2008)²¹⁴ who reviewed measures for the hemiparetic upper limb. This review identified six scales that met their selection criteria, but concluded that currently there was no single reliable and valid measure available to capture the full range of functional tasks in the hemiparetic upper limb. This type of systematic review provides invaluable information but also raises important questions. For example, how well targeted are different measures to the goals of specific interventions? How do we select

the best available measures for future clinical studies? What criteria should be used and why?

A systematic review and scale selection strategy was therefore carried out to select the most scientifically sound and clinically relevant outcome measures to evaluate the studies performed in this thesis. This was carried out by the use of three stages: First, two psychometric guidance documents that define key scale assessment criteria were reviewed, Second, consideration was given, at a theoretical level, to clinical issues, concepts, and domains important to include in stroke outcome research. Thirdly a comprehensive literature review was performed and reviewed with input from healthcare professionals, psychometricians, and librarians.

4.3 STEP I: PSYCHOMETRIC GUIDANCE DOCUMENTS

The two most widely used guideline documents for psychometric standards for rating scale research were selected, to provide appropriate criteria against which to examine existing scales. First, the Scientific Advisory Committee of the Medical Outcome Trust ²⁴⁶(MOT) guidance for the development and validation of patient reported outcome (PRO) measures. Second, the US Food and Drug Administration (FDA)²⁴⁷ guidelines for PRO measures in clinical trials. Both the MOT and FDA documents emphasize the importance of patients' views in clinical research.²⁴⁸ Both documents identify key properties for psychometrically robust measures. Table 4.1 and. 4.2 summarizes the key issues identified by the documents (ie data quality, scaling assumptions, targeting, reliability, validity and responsiveness). Taken together these documents provide an essential basis in the process of selecting PROM because they provide rigorous standards that scales should meet. It is important to note that these properties of a PROM also have relevance to clinician-rated scales, which should be evaluated in the same rigorous manner.²⁵⁸

Table 4.1: 8 key “attributes” when designing outcome measures, as detailed in MOT²⁵⁹

<i>Attribute</i>	<i>Properties</i>
Conceptual and measurement model	Rationale for and depiction of the concept(s) the measure is intended to assess (e.g., scale and subscale structure)
Reliability	Degree to which the measure is free from random error, including internal consistency and test-retest reproducibility
Validity	Degree to which instrument measures what is purports to measure, including content, construct, and criterion validity
Responsiveness	Instrument's ability to detect change in outcomes that matter to persons with a health condition, their significant others or their providers
Interpretability	Degree to which one can assign clinical or commonly understood meaning to quantitative scores
Respondent and administrative burden	Time, energy, and other difficulty placed on respondents and on those who administer the instrument
Alternative forms	Equivalent information on versions of measures other than original source
Cultural and language adaptations (translations).	Conceptual and linguistic equivalence and psychometric properties of cross-cultural adaptation

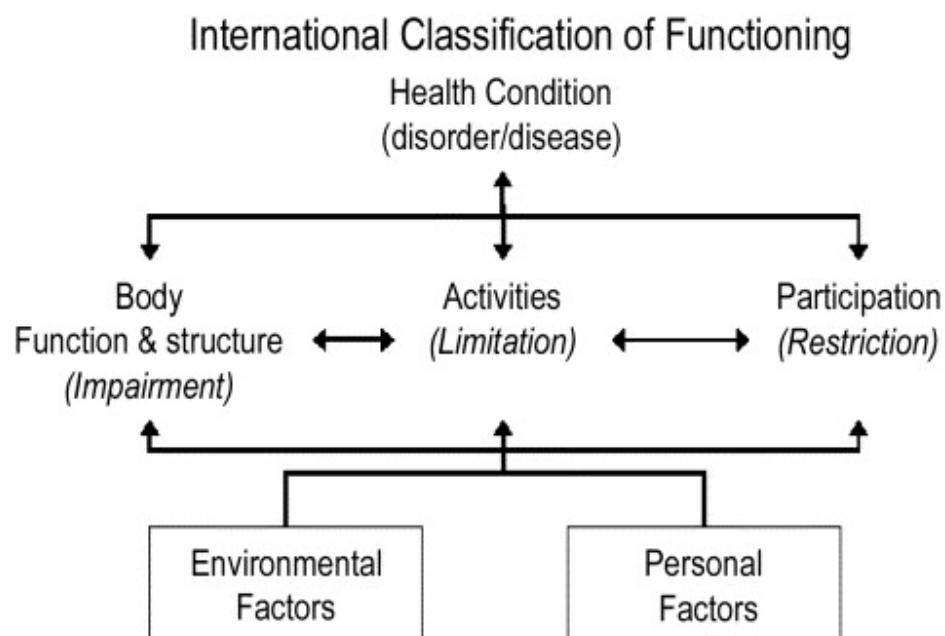
Table 4.2: Summary key issues in FDA guidelines (adapted from Cano& Hobart (2008)²⁶⁰)

<i>Psychometric property</i>	Definition
Data quality	Assessed by completeness of data and score distributions
Scaling assumptions	<ul style="list-style-type: none"> • Items in a scale should measure a common underlying construct • Items in a scale should contain a similar proportion of information concerning the construct being measured • Items should be correctly grouped into scales
Targeting	<ul style="list-style-type: none"> • Indicates whether a scale is acceptable as a measure for the sample
Reliability Internal consistency Test–retest reproducibility	<ul style="list-style-type: none"> • The extent to which items in a scale measure the same construct • The stability of a scale between repeat administrations of the scale on two occasions

4.4 STEP II: STROKE-SPECIFIC ISSUES IN THE SELECTION OF APPROPRIATE OUTCOME MEASURES

There is no consensus on the battery of outcome measure to use when assessing physical recovery post-stroke. Selecting the appropriate scales to assess recovery in stroke is a difficult task given the heterogeneity of stroke aetiology, symptoms, severity, and even recovery itself. However, despite these complexities, several clinically anchored strategies can assist in selecting the right measure for this population in clinical research. Thus, in addition to the psychometric guidelines described above, the International Classification of Functioning, Disability and Health (ICF)²⁶¹ framework was also included to help identify scales with relevant domains for the studies.

Figure 4.1: ICF Model ²⁶¹



The ICF framework provides a conceptual framework for the selection and classification of outcome measures. The domains contained in the ICF include Body Functions and Structures (impairments) and Activities and Participation (disabilities):

- **Body functions and structures:** This refers to physiological functions of body systems including psychological. Structures are anatomical parts or regions of body and their components. Impairments are problems in body function or structure.
- **Activity:** activity refers to execution of a task by an individual .Limitations of a task are defined as difficulties an individual might experience in completing a given activity.
- **Participation:** involvement of an individual in a life situation. Restrictions to participation describe difficulties experienced by the individual in a life situation or role.
- **Contextual factors:** these include personal and environmental factors that influence the relationship between the different components

The impacts of stroke on the domains of the ICF are not always directly related to each other. The severity of impairment does not necessarily determine the limitation in activities and participation due to the varied interplay between these domains and the influence of contextual factors.²⁶² Such differences may also be seen in relation to the effects of any intervention (e.g. changes at the impairment level do not necessarily translate into the other domains, e.g. participation)

Measures of impairment have been postulated to be the best markers of prognosis ²⁵⁴ Impairment scales may be the most sensitive to change and have the greatest capacity to differentiate between treatment groups. However, for clinical significance and health policy it is important to relate changes in impairments to changes in activity and participation. Activity measures are the most frequently used primary outcome measures in stroke. The most common domain of activity measurement is basic activities of daily living (ADLs)²⁶³.However, it has been found in studies of unselected stroke population, that approximately 60% of the patients will make a “complete recovery” in basic ADL ²⁶³.This means that ADL measures are subject to ceiling effects and may therefore not show a difference between groups in outcome, significantly reducing the power of any study²⁵⁴.

A challenge in all activity and mobility measures is that the link between the extent of loss at the level of pathology and impairment is not perfectly correlated and other factors may

influence the outcome²⁶². For example, an individual may improve in motor function, but without good social support to encourage independence, he or she may not resume social roles, such as being a grandparent or going out with friends.. Although there is a growing call to include participation measures as an important component of disability. Few measures look at this aspect.

In the context of upper limb rehabilitation post stroke research, it may be important for researchers to know what impact an intervention has had at an impairment level, but it is equally important to identify what impact these changes have for individuals at an activity or participation level and how this affects more complex multidimensional concepts such as quality of life²⁶⁴.

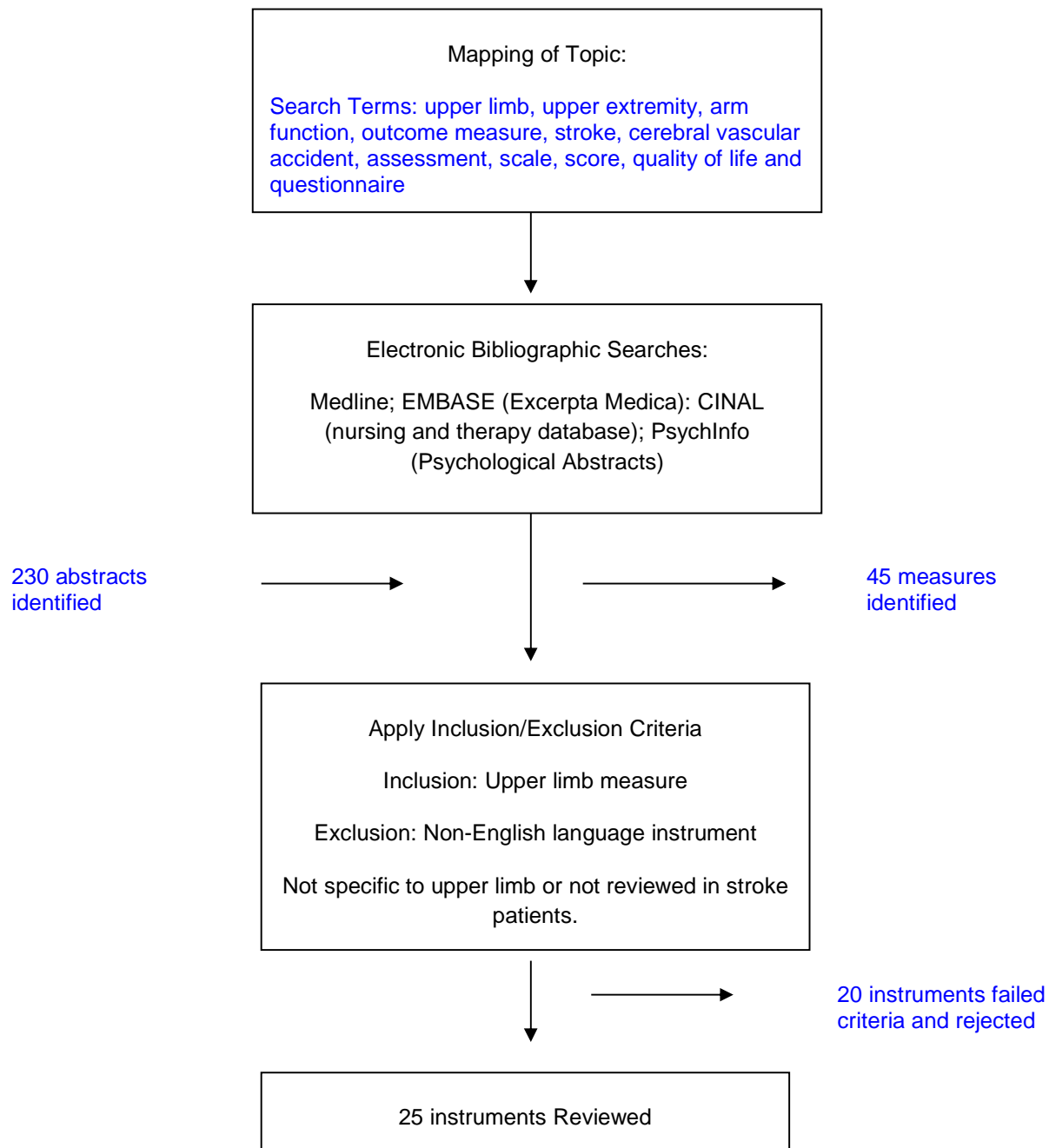
Novel treatments need refining until their impact at the level of body structure and function translates into something meaningful for the patient. The studies outlined in this thesis used stroke survivors ranging from those with only a few proximal shoulder flickers to those with near normal arm strength. To appropriately assess ReachMAN, scales were required that captured clinically important improvements in arm movements at all levels of the ICF. This is endorsed by Sivan et al (2010)²⁶² who concluded in their review of the outcome measurement used in clinical literature investigating robotic devices that a basket of outcome measures covering all domains of ICF is crucial, as it is important to measure change in each domain.

4.4 STEP III: LITERATURE REVIEW

A comprehensive literature search strategy and review were developed in conjunction with healthcare professionals (the author of this thesis (KB) and Dr Diane Playford), psychometricians (Stefan Cano), and a librarian (Kate Brunskill). An electronic bibliographic search was conducted in the following databases: Medline, Embase (Excerpta Medica), CINAHL, and PsycINFO. The databases were searched from 1966 to 2011. Limits were placed on each search to exclude non-English citations and nonhuman subjects using a variety of key terms, including upper limb, upper extremity, arm function, outcome measure, stroke, cerebral vascular accident, assessment, scale, score, quality of life, and questionnaire. All instruments included in the review were identified as an upper limb outcome measure. A follow-up review of references was performed to find relevant

articles not detected in the electronic searches. From this search, scales that measure global motor function but also included a specific upper limb subsection were included (eg, the Rivermead Motor Assessment). However, scales in which upper limb function was not separate from other functions were excluded (eg, the Stroke Impact Scale). Scales that had not been psychometrically evaluated in patients with stroke were also excluded. Figure 4.2 illustrates this search.

Figure 4.2: Flow diagram of systematic literature review carried out to identify upper limb outcome measures



4.4.1 RESULTS OF THE LITERATURE REVIEW

The findings from the literature review were cross-referenced against the guideline documents criteria and clinical considerations underpinned by the ICF framework. The review itself identified 25 outcome measures used to evaluate upper limb recovery post stroke. These measures were separated into stroke-specific clinician-rated and PROM. The properties and initial evaluation of these 25 measures against the specific criteria identified on the MOT/FDA guidance are shown in Table 4.3 and 4.4. Three measures were identified that best met the criteria of the MOT and FDA guidelines: Chedoke Arm and Hand Inventory, Stroke Rehabilitation Assessment of Movement upper limb section, and ABILHAND. Details regarding the development and psychometric properties of these measures are described below. A fourth measure, the Upper Limb– Motor Assessment Scale, also fit many of the MOT criteria, but a closer inspection of psychometric properties of the measure found that the upper limb items should be used with caution. This scale was therefore not felt to be suitable for use in our study. A summary of the three identified measures is presented below. (Appendix 111 describes psychometric criteria used for evaluation of the measures).

Table 4.3: Stroke clinician rated scales: Development and validation criteria

	ARAT	CAHAI	10-s test	AMAT	WMFT	FMA	MSS	UL-MAS	DeSouza	RMA	STREAM	MESUPE	Motricity Index	NHPT	FAT	Sodring	Sollerman	MCA	MMAC	Box and Block	Functional
Item Generation																					
Patient Interviews		♦																			
Literature		♦						♦			♦										
Expert opinion		♦						♦			♦										
Develop conceptual model																					
Item Reduction																					
Expert opinion		♦									♦										
Item redundancy		♦									♦										
Endorsement		♦																			

	ARAT	CAHAI	10-s test	AMAT	WMFT	FMA	MSS	UL-MAS	DeSouza	RMA	STREAM	MESUPE	Motricity Index	NHPT	FAT	Sodring	Sollerman	MCA	MMAC	Box and Block	Functiona I
frequencies																					
Missing data		♦																			
Factor analysis																					
Tests of scaling assumptions																					
Psychometric Analyses																					
Acceptability																					
Internal consistency reliability		♦		♦	♦	♦	♦	♦		♦	♦	❖									
Item total correlations												❖									

	ARAT	CAHAI	10-s test	AMAT	WMFT	FMA	MSS	UL-MAS	DeSouza	RMA	STREAM	MESUPE	Motricity Index	NHPT	FAT	Sodring	Sollerman	MCA	MMAC	Box and Block	Functiona I
Inter -rater reliability	♦	♦		♦	♦	♦	♦	♦		♦	♦									♦	♦
Test-retest reliability	♦	♦		♦	♦	♦	♦	♦		♦	♦		♦	♦	♦		♦			♦	
Validity: within scale	♦	♦				♦		♦		♦	♦	❖		♦	♦		♦				
Validity: comparison with other measures	♦	♦	♦	♦	♦	♦	♦	♦	♦	♦	♦		♦	♦	♦	♦	♦		♦	♦	
Validity: hypothesis Testing																					
Responsiveness	♦							♦			♦									♦	

Key:ARAT, Action Research Arm Test; CAHAI, Chedoke Arm and Hand Inventory;10-s Test, 10 second Tests; AMAT, The Arm Motor Ability Test; WMFT, Wolf Motor Function Test;FMA,Fugl-Meyer Assessment; MSS, Motor Status Score; UL-MAS, upper limb of Motor Assessment Scale; Dezouza, Dezouza arm Test; RMA, Rivermead Motor Assessment: STREAM, stroke rehabilitation assessment of movement, MESUPE. Motor Evaluation Scale for the Upper Extremity in Stroke Patients; NHPT, Nine Hole Peg

Test, FAT; Frenchay Arm Test; Sodring, Sodring Motor Evaluation Test, Sollerman, Sollerman Hand Function Test; MCA, Motor Club Assessment, MMAC, Modified Motor Assessment Chart

❖ - As defined by Rasch analysis using RUMM 2010 software.

Table 4.4: Stroke Patient Reported Outcome Measures: Development and validation criteria

	DHI	MAL	ABILHAND	UMAQS
Item Generation				
Patient Interviews			♦	
Literature			♦	
Expert opinion			♦	
Develop conceptual model			♦	
Item Reduction				
Expert opinion			♦	
Item redundancy			♦	
Endorsement frequencies			♦	
Missing data			♦	
Factor analysis			♦	
Tests of scaling assumptions			♦	
Psychometric Analyses				
Acceptability			♦	
Internal consistency reliability	♦	♦	♦	
Item total correlations		♦	♦	
Inter -rater reliability			♦	
Test-retest reliability	♦		♦	♦
Validity: within scale		♦	♦	
Validity: comparison with other measures	♦	♦	♦	
Validity: hypothesis testing			♦	
Responsiveness	♦		♦	

Key: DHI-Durvoz Hand Index, MAL-Motor Activity Log, ABILHAND-ABILHAND Questionnaire, UMAQS- University of Maryland Arm Questionnaire for Stroke

4.4.2 IDENTIFIED SCALES FROM THE INITIAL LITERATURE REVIEW

CHEDOKE ARM AND HAND INVENTORY²⁶⁵

Purpose: This measure was developed methodically to look at functional tasks post stroke. Initially 109 stroke patients and their carers were interviewed and from this literature review and expert opinion 751 items were generated. Item reduction was then carried out by statistical analysis and expert opinion as well as piloting the measure.

Content: The test consists of thirteen real-life functional tasks that reflect domains deemed important by survivors of stroke. This included (1) bilateral activities (2) non-gender specific tasks, (3) the full range of movements, pinches and grasps and (4) covering all stages of motor recovery post stroke²⁶⁶

Psychometric data: The development ensured face, content and factorial validity. Convergent validity with the ARAT ($r = .93$) and the CMSA ($r = .87$) were high. Internal consistency ($r = .98$) and single item factor loading are high (range .76-.96). Interrater reliability was high (ICC .98)²⁶⁵.

STREAM²⁶⁷

Purpose:

Provides a comprehensive, objective and quantitative evaluation of motor functioning of individuals with stroke.

Content: Consists of 30 items that are distributed among three subscales, Upper Limb movements, Lower limb movements and basic mobility items. Limb movements are scored on a 3 point scale, while mobility items are scored on 4 point scale. There is a maximum score of 70 with each limb subscale scored out of 20.

Psychometric Properties: Reliability and Validity has been established. Inter and intrarater reliability correlation coefficients of .99 (total score), .96 to .99 for subscores. Internal consistency in 26 patients was found Cronbach alpha $> .98$ ²⁶⁸. Wang et al (2002)²⁶⁷ on 54 patient's found inter rater reliability weighted kappa of individual items ranged 0.55-0.94,

intraclass correlation co-efficient total score was 0.96 and was also high in the subscales (UL scale 0.95). Concurrent validity against Barthel Index and FMA has found a spearman rho 0.67 and 0.95, and against FMA-UL subscale $r = 0.87$. Ahmed et al (2003)²⁶⁹ looked at validity against various measures including Box and Block and found Pearson coefficient 0.57 to 0.80. Predictive validity was comparable to BI and gait speed. The authors²⁶⁹ found responsiveness mean estimate supported the ability of the STREAM to reflect change over time.

Rasch analysis has also been performed on this measure, using WINSTEPS software.²⁷⁰ After deleting items from scale to fit the model, the shortened measure was found to demonstrate high Rasch reliability, unidimensionality, and concurrent validity in patients with stroke.

4.4.3 PATIENT REPORTED MEASURES

ABILHAND²⁷¹

Purpose: This was initially devised to measure “manual (dis) ability in patients with Rheumatoid arthritis who had undergone arthrodesis. The test was then looked at in chronic stroke patients. The measure was devised using Rasch.

Content: “ABILHAND” is an inventory of 56 manual activities that patients were originally asked to judge on a 4 level scale: 0 (impossible), 1 very difficult, 2 difficult, and 3 easy. The test explores both unilateral and bimanual activities done without other human help. For each question the patient provided his/her feeling of difficulty irrespective of the limb actually used to do the activity.

Psychometric data: The ABILHAND was initially analysis with use BIGSTEPS Rasch analysis computer software, in a group of patients with rheumatoid arthritis. The scale was then adapted for chronic stroke using the Winsteps Rasch analysis computer program. The measure was found to have a Rasch reliability of 0.90, and item-difficulty hierarchy was stable. ²⁷¹

Table 4.5: Classification of UL outcome measures in the ICF framework

Impairments	Activity	Participation
STREAM	CAHAI	ABILHAND

4.5 ADDITIONAL SCALES

There were immediate drawbacks to using the three identified scales in isolation. All are relatively new scales that have not been widely used in the upper limb intervention trial literature. Using these scales alone would have made it difficult to compare the results of the studies with others in the stroke literature. Therefore, it was felt to be appropriate to add further scales that would address this key point but would still be psychometrically valid and cover impairment and activity. From the initial electronic bibliographic search, two further measures of impairment were selected. The FMA upper limb section and ARAT were chosen because they have been widely used in the robotic stroke literature and have been used as “gold standard” for comparison with other measures. A summary of these measures follows.

FUGL-MEYER ASSESSMENT (FMA)²⁷²

Purpose: This impairment based measure was developed to assess motor recovery following stroke and was based on early works of Twitchell²⁷³ and Brunnstrom²⁷⁴. It is widely used in stroke research and has been used as a gold standard to compare the reliability and validity of other outcome measures.

Content: Scoring ranges from 0 to a maximum of 66 for upper limb movement. The upper limb section has 33 items, which include reflex testing, movement observation, grasp testing and assessment of co-ordination.

Psychometric data: The validity, reliability and responsiveness of the FMA have been extensively reported. Concurrent validity has been demonstrated with the MAS ($r = .64-.92$ ²⁷⁵, each subscale of the ARAT (functional ability, $r = .94$, quality of movement = $.94$)²⁷⁶, and

the Barthel Index ($r=.75$) Intra-rater reliability ($r=.995$) and inter-rater reliability ($r=.992$)²⁷⁷ test-retest reliability (intraclass correlation coefficient, $.94-.99$)²⁷⁸, along with internal consistency ($r=.97$)²⁷⁹ have been found to be excellent.

Rasch analysis has been performed on the FMA upper limb section²⁸⁰. Woodbury et al (2007)²⁸⁰ who conducted this analysis concluded that based on Rasch model criteria as operational by Winsteps software the items testing reflexes may threaten the assessments dimensionality. The Rasch –item difficulty order was not consistent with the hierarchical structure and item order of the measure. A modified FMA was found to show a longitudinally stable item difficulty order.

ACTION RESEARCH ARM TEST (ARAT): -

Purpose: This measure was devised in 1965 as the upper extremity function test (U.E.F.T), it was developed by testing on 200 people with UL difficulties with the objective of developing a testing procedure that was representative of the major activities of the upper limb in everyday activities of daily living²⁸¹. The test was reorganised by Lyle (1981)²⁸² to look specifically at UL dysfunction post cerebral cortical injury, using a Guttman scale and renamed “ARAT”. The test has been widely used in rehabilitation and treatment trials.

Content: The ARAT is a performance test that consists of 4 domains: grasping (lifting up different size objects), gripping (holding and moving objects), pinching (picking up small objects) and gross movement (e.g. hand to mouth) involving 19 movements.

Psychometric data: Just as the FMA, this measure has been extensively examined against other measures, and is used as a ‘gold standard’ for the comparison of other upper limb measures (64-69). The measures reliability, validity and responsiveness have been extensively examined and established. Interrater reliability ($.98$) and test-retest reliability ($.99$) have been established^{283 284}. Concurrent validity of the ARAT with the Fugl-Meyer Assessment (r range $.91-.94$)^{276 285}, the ARAT and the Motor Assessment Scale, upper extremity part ($r=.96$)²⁸³ and the ARAT and the Motricity Index has been demonstrated ($r=.87$)²⁸³. Various authors have found that the ARAT is responsive to change (effect size greater than 1.0)^{284 285},

The scale unidimensionality has been validated by Mokken analysis (a non-parametric item response theory model).²⁸⁶ Koh et al (2006)²⁸⁶ also examined the parametric

function of ARAT by Rasch analysis using WINSTEPS program. This analysis produced poor Rasch model–data fit, suggesting that the raw scores of the ARAT cannot be transformed into interval scores and do not represent patients exact functioning. From this analysis Koh et al (2006)²⁸⁶ advise that interpreting the difference in scores should be interpreted with great care.

4.6 SCALE EVALUATION - CLINICAL CONSIDERATIONS

At this stage measures had been identified that were: 1. Psychometrically robust, 2. In common usage and 3. Evaluated a range of impairments. A measure of activity had been identified and one of participation that although psychometrically robust were used rarely. However scales had not been identified that quantified the severity of the stroke, the impact of stroke on daily life or measured quality of life. Therefore a consideration was given to a number of measures that were more generic, and thus not identified in the original literature review, but are familiar because they are in common usage. These included the National Institutes of Health Stroke Scale the SF 36, Barthel index and EQ-5D. The EQ-5D was also included to allow assessment for health economics. (as recommended by Sivan et al (2010)²⁶²). A further PROM specific upper limb measure the Disabilities of the Arm Shoulder and Hand (DASH) was also included. This was included as although this measure has not been widely used in stroke or robotic research the measure has undergone extensive psychometric testing and is a measure of everyday active arm function.

Further specific search targeting the psychometric properties of these scales was conducted and detailed below: The levels under ICF framework that the added scales fall under is seen in Table 4.6.

NATIONAL INSTITUTES OF HEALTH STROKE SCALE (NIHSS)²⁸⁷

Purpose: The NIHSS was initially designed to assess differences in interventions in clinical trials, although it has also been used as an initial assessment tool. The scale was designed to evaluate neurologic outcome and degree of recovery for patients with stroke. It was based on three previously used scales, the Toronto Stroke Scale, the Oxbury Initial Severity Scale and the Cincinnati Stroke Scale²⁸⁷

Content: The NIHSS is a 15-item scale, which assesses level of consciousness, extraocular movements, visual fields, facial muscle function, extremity strength, sensory function, coordination (ataxia), language (aphasia), speech (dysarthria), and hemi-inattention (neglect).

Psychometric Properties: Reliability, validity and responsiveness have been investigated in the scale and match recommended criteria. Test-retest reliability of the original NIHSS was reported as adequate to excellent²⁸⁷. The inter-rater reliability and intra-rater reliability has been established.²⁸⁸ The validity of the scale has been looked at with the Modified Rankin Scale and Barthel Index and Glasgow Outcome Scale²⁸⁸... The NIHSS was found to predict against these other measures at 3-month outcome. No studies have examined the internal consistency of the NIHSS. A significant ceiling effect has been detected with the NIHSS.^{289;290}

SF-36²⁹¹

Purpose: The Medical Outcomes Study 36-item Short-Form Health Survey was developed as part of the Medical Outcomes Study (a two-year study of patients with chronic conditions)²⁹¹

Content: The SF-36 consists of 11 questions, with 36 items in total. With the exception of the general change in health status questions, subjects are asked to respond with reference to the past 4 weeks. An acute version of the SF-36 refers to problems in the past week only. Items of the SF-36 are divided into eight different domains: Physical component which consists of Physical functioning, role limitations due to physical problems, bodily pain, and general health perception; Mental component which is broken down to items of social functioning, general mental health, role limitations due to emotion problems and vitality. Respondents are also asked to rate their current health status compared to their health status one year ago.

Psychometric Properties: The reliability of the measure match recommended criteria, although no studies have examined the inter-rater reliability of the measure. The validity of the measure has been questioned in stroke with five of the eight SF-36 subscales were found to have limited validity as outcome measures, and that the reporting of physical and mental summary scores were not supported.²⁹² These findings have been disputed by De Haan.(2002) ²⁹³ Rasch analysis has been performed on the measure examining the unidimensionality and differential item functioning of the physical functioning subscale of scale.²⁹⁴ For some items differential item functioning was seen for the stroke sample compared with other neurological conditions.

EQ-5D²⁹⁵

Purpose: The EQ-5D was developed by an international and interdisciplinary group of researchers (EuroQol Group) in 1987. The scale was devised to produce developing a standardized non-disease-specific instrument for describing and valuing health-related quality of life. The score can be used as weights for calculating quality-adjusted life years.

Content: The EQ-5D questionnaire is a simple generic instrument which consists of 5 dimensions mobility, self-care, usual activities, pain/ discomfort and anxiety/depression. Subjects have to choose the level that best describes their health status on each dimension. Each subject's health status is described as a combination of five digits (one for each dimension rated), and the EQ-5D descriptive system generates 243 different health states.

Psychometric Properties: The reliability, validity and responsiveness have been examined and match criteria. The measure has been assessed against many other measures including SF-36. Ceiling effects have been found with the measure.

BARTHEL INDEX²⁹⁶

Purpose: The Barthel Index was first developed by Mahoney and Barthel ²⁹⁷in 1965 and later modified by Collin et al in 1988²⁹⁶. The index was developed for use in rehabilitation patients with stroke and other neuromuscular or musculoskeletal disorders. A number of version of the index exist, with no consensus over which should be considered the definitive version of the Barthel Index , but the original and the 10-item and 15-item modifications are the most commonly used.

Content: The index measures the extent to which somebody can function independently and mobility in their activities of daily living (ADL) i.e., feeding, bathing, grooming, dressing, bowel control, bladder control, toileting, chair transfer, ambulation and stair climbing. The index also indicates the need for assistance in care.

Psychometric Properties: Reliability, validity and responsiveness have been found to match evaluation criteria . Inter rater reliability has also been established.²⁹⁸ Concurrent validity of

the index with the SF-36, Berg balance scale, FMA and Frenchay Activities Index has been demonstrated.²⁹⁸ The measure has been found to have significant ceiling effects²⁹⁹

DISABILITIES OF THE ARM SHOULDER AND HAND (DASH)³⁰⁰

Purpose: A region specific measuring tool to measure outcome of musculoskeletal conditions affecting the upper limb³⁰⁰ The measure was methodically developed using a group of methodologists and clinical experts. Item reduction was then carried out via extensive field-testing in patients. It has been used widely as a measure for conditions of the hand, wrist, elbow and shoulder.

Content: It is a 30-item questionnaire, which measures physical, and social functions together with symptom impact. There are optional sport/music and work specific sections. Each question is scored by a five point Likert scale and scores are summed with a lower score indicating less disability. An 11 item Quick DASH has also been developed, using the most sensitive and responsive questions³⁰¹ This measure is being increasingly used in research regarding neurological impairment.

Psychometric Properties: Atroshi et al (2000)³⁰² looked reliability and validity in patients with surgical and non-surgical musculoskeletal disorders. Internal consistency was high (alpha:0.96), as was test-retest reliability (ICC:0.96).³⁰² Validity has also established, with Beaton et al (2001)³⁰¹ finding good correlation with DASH, the Bringham (carpal tunnel) questionnaire, the SPADI (Shoulder Pain and Disability Index), and other markers of pain and function ($r > 0.69$.)

4.6.1 LIMITATIONS OF THE ADDITIONAL SCALES SELECTED.

When looking at the psychometric properties of the above measures it was clear that there are weaknesses in the measures. In an ideal situation more robust psychometric measures would be used. However on a pragmatic level the use of these measures allowed comparability, meta analysis and cost effectiveness analysis.

Table 4.6: Classification of measures in the ICF framework

Impairments	Activity	Participation
NIHSS	Barthel Index	SF 36
FMA	ARAT	EQ-5D
		DASH

4.7 CONCLUSION

To identify the most appropriate outcome scales for the studies in this thesis a three stage approach was used: firstly best practice psychometric guidelines were used to evaluate measures, these were then compared against a theoretical framework and clinically important criteria. The scales were then categorized into the ICF framework to ensure clinical relevance. 'Gold standard' measures and measures of wide spread use were also included to ensure the results were understood by the wider research community and were reproducible. Using this method, the above scales were chosen to be used in this research trial: STREAM, CAHAI, ABILHAND, FMA, ARAT, EQ5D, SF36, Barthel Index, NIHSS and DASH. These scales represent not only all domains of the ICF framework but also incorporate a mixture of clinical rated and patient reported outcome measures.

The scale selection strategy described in this chapter highlighted that current rating scales have their limitations. With the example of scales for the hemiparetic upper limb, there is currently no single valid and reliable scale available to portray the complete range of function in the arm²¹⁴. Scales that look at the participation component of the ICF are

extremely limited. Furthermore, studies have used scales that have been found to be psychometrically restricted. However, it was felt that the studies described in this thesis needed to use scales that covered a wide range of activities, and ICF domains, even if the scales had weakness. This was also to allow the studies to be compared and amalgamated using meta-analysis with other robotic studies.

4.8 SUMMARY

This chapter has discussed the scale selection strategy used in the identification of outcomes for the studies in the thesis. The following chapters will describe fully the methodologies used in each of the stages of the study and the results that they generated as well as implications for practice.

CHAPTER 5- A RECRUITMENT STUDY (PHASE 1).

5.0 INTRODUCTION

Motor deficit of the upper limb is common after stroke and severe impairment is prognostic of poor recovery ⁷⁴. Although a range of therapeutic techniques is used, most of these interventions (e.g. CIMT, task specific training) rely on the presence of at least some active movement. A number of experimental techniques are currently being investigated such as the use of robotic devices, however, these are not yet integrated into routine clinical practice. At present there is little therapy specifically to promote recovery of the severely paretic or paralysed upper limb after stroke.

The clinical trials that have looked at the use of robotic devices in the acute and subacute population suggest that this adjunct may improve motor performance post stroke (as discussed in greater depth in Chapter Two). In order to evaluate this further and in particular assist in the integration into clinical practice, the present study was designed to establish the proportion of acute stroke patients who could potentially benefit from rehabilitation using a robotic device. The study was designed to comply with the MRC (2008) guidance It may be defined as Phase II (modeling) study.

The aims of this first phase of the study were:

5.1 AIMS:

- 5.1.1 Determine future recruitment criteria
- 5.1.2 Determine the rate and timing of recruitment in practice
- 5.1.3 Make recommendations about choice of outcome measure for the second phase of the study-the exploratory RCT.

5.2 RESEARCH QUESTIONS

- 5.2.1 What are the inclusion and exclusion criteria for an exploratory RCT?
- 5.2.2 How many people would be able to use a mock up of the device and how long does this take to recruit in practice?
- 5.2.3 Are the outcome measures feasible and practical to use?

5.3 METHODOLOGY

5.3.1 PATIENT SELECTION

The initial plan was to recruit one hundred consecutive single incident stroke patients admitted to UCLH NHS Trust, provided they were capable of giving informed consent. The criteria for inclusion and the actual number of patients recruited is discussed in more detail in section 5.4

5.3.2 SETTING

Recruitment into this study commenced in July 2009. At that time people with suspected strokes were admitted to UCLH Accident and Emergency department and then transferred to a designated ward in the hospital. In 2010 UCLH, was designated as one of eight hyper-acute stroke units (HASUs) in London and the only one in the North Central London. This formed part of Healthcare for London's plan for the improvement in the quality of stroke care. HASU admits acute stroke patients from across North Central London. This HASU see about 160 patients each month, about 80 of these are strokes. HASU provides rapid assessment, thrombolytic and interventional treatment to patients in the hyperacute phase following stroke. Most patients who have been diagnosed with a stroke stay for 72 hours on HASU before being transferred to their local stroke unit or discharged home.

5.3.3 PATIENT RECRUITMENT

All patients who were admitted to UCLH NHS Foundation trust who were confirmed to have had a stroke (confirmation of stroke either seen on CT/ MRI scan or by clinical symptoms, the diagnosis being made by specialist stroke consultants) were notified to the research physiotherapist (KB) by a research nurse. The responsible clinician was then asked for permission to approach the patient.

Initial inclusion criteria for the study were:

1. Able to give informed consent
2. Single incident stroke, within the last seven days.

Recruitment of this phase of the study began in July 2009. It became clear from the onset that excluding people from the study who had had subsequent strokes was an oversight as this may have missed the large number of patients with second strokes who could also benefit from using the robotic aid. In retrospect, the decision to exclude second strokes seemed somewhat arbitrary. Therefore an amendment to the ethical approval protocol for the study was applied for and obtained in December 2009. This amendment therefore meant that anyone within seven days of having a new stroke would be eligible to be recruited. Recruitment was to continue until 100 single incident strokes were recruited.

5.3.4 STUDY INFORMATION

The information sheet for participants was written using UCLH guidelines; this sheet gave them further information about the study, possible interventions and how the data collected would be used (see Appendix IV). Each participant read the information sheet prior to agreeing to participate in the study. Once verbal agreement was reached a consent form was then signed. The consent form was developed using UCLH guidelines and National Research Ethics Service guidelines (see Appendix IV).

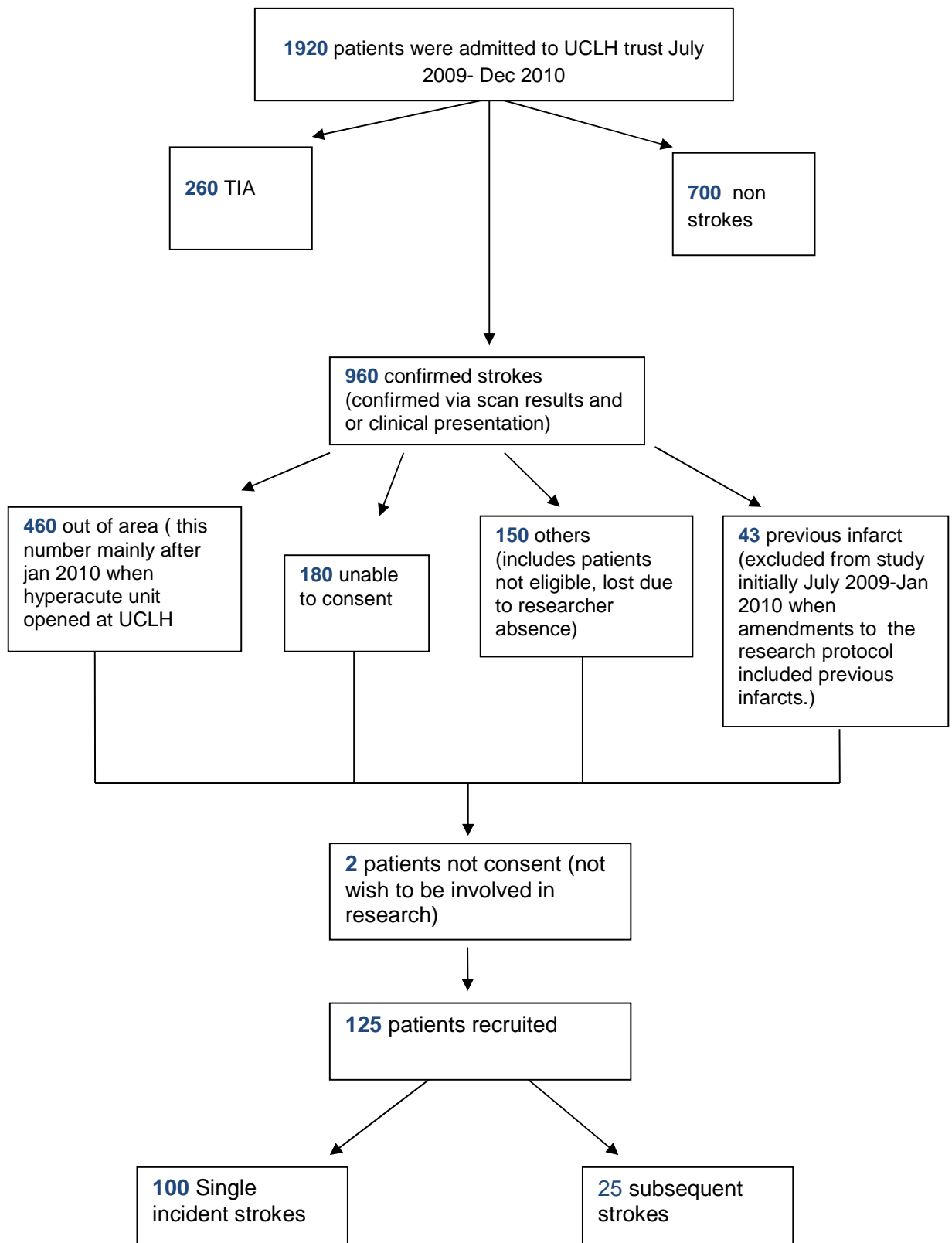
5.3.5 ETHICAL APPROVAL

Ethical approval for the study was obtained from the joint research ethics committee of the NHNN and the ION (see Appendix V) (Approval number 08/H0716/13). All participants gave their informed written consent.

5.3.6 PROCEDURE

Screening was undertaken by the Research Therapist, following notification of new strokes admitted into HASU by the stroke research nurse. Ward lists were reviewed on a regular basis, the MDTs were consulted regarding the suitability of people for the trial, and medical notes were screened for all those diagnosed with a confirmed stroke. The Research Therapist also attended ward rounds if able. Wherever possible, the Research Therapist was introduced to potential participants by a member of the MDT. A verbal explanation of the trial was given to the individual (and also to their relatives and friends, when they were present). This was supported by the provision of the Patient Information leaflet. Individuals were encouraged to discuss their participation with family/friends/members of the MDT, and to ask questions about the trial. It was stressed that the individual could withdraw from the trial at any stage and that participating would not affect their usual care. The Research Therapists, family and friends of the individual, and the Speech and Language Therapists supported people with aphasia in the consent process. Informed consent was taken by the Research Therapists, a copy of the consent was given to the individual and a copy was placed in their medical records.

Figure 5.1: Flow Diagram to Show the Recruitment Process



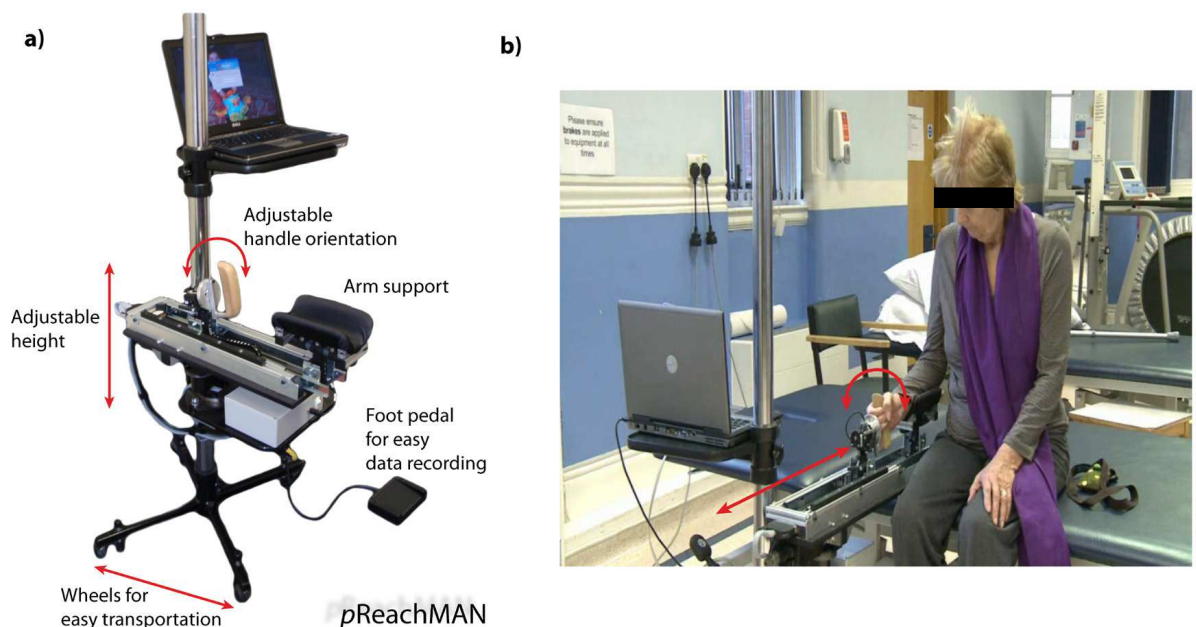
5.3.7 INTERVENTION

Patients were assessed by the Research Therapist within seven days of admission. This assessment consisted of a series of Patient Reported outcome measures and Clinician Rated outcome measures. These measures have been described in detail in Chapter Four.

If the patient had any difficulties with using their arm they were seen weekly for six weeks or until they were discharged. All patients with upper limb problems were re assessed at six weeks. This assessment either occurred at UCLH, the Acute Brain Injury Unit at NHNN or the patient was seen at home.

The patients who were seen to have upper limb problems were seen weekly until discharge. During this weekly visit, their ability to interface with a 'mock up' of the robotic aid was assessed. This device is shown in Figure 5.2 (this mock up device was named pReachMan).

Figure 5.2: Illustration of the mock up robotic device (pReach MAN): a) Photograph of the device b) A subject using the device.



The pReachMan device has no actuated motors. The device is equipped with sensors that allow kinematic and dynamic data to be saved and monitored with a standard PC or a laptop. Patients can see visual graphs when they perform movements with the device. pReachMan was set up to record impairment level information including the range (i.e. position) and strength (i.e. force/torque) of the following movements: supination, pronation of the forearm and extension and flexion through the elbow and shoulder.

Subjects were set up and trialed to use the device on a weekly basis if possible. (pReachMan was designed by Dr Alejandro Medendez in 2009 who designed the machine as a part of his Phd thesis from Imperial College. He describes the design of the device in his thesis ³⁰³)

5.3.8 ANALYSIS

Descriptive analysis of the numbers of people admitted to UCLH trust over the time period of the study was undertaken and the numbers of strokes who matched the recruitment criteria. A further descriptive analysis was undertaken of the number of stroke participants who had upper limb deficits and who were able to interface with the robotic device.

Outcome measures were recorded for all participants. This was to evaluate the feasibility and acceptability of the measures for the next stage of the study (the exploratory RCT). Furthermore this was also to allow psychometric analysis of the measures. This analysis will be discussed in detail in Chapter Eight.

5.4 RESULTS

Recruitment into this stage of the study occurred from July 2009 until December 2010. Figure 5.2 illustrates the recruitment process into the study. During the time period 1920 patients were admitted into trust. 260 of these patients were diagnosed with TIA and therefore did not meet the study criteria, while a further 700 were found to have not had a stroke. These again were excluded from the study. Of the remaining 960 patients who were confirmed as stroke, 460 of these were out of area. This meant that following their

initial presentation and admission to HASU they were then transferred to a hospital outside of UCLH trust within seven days of surviving a stroke. These patients were not able to be followed in their new destination as the study was for single site ethics approval only. The majority of these patients were lost to the study after January 2010, when the HASU was opened, as this new unit covered people from the entire North London sector. Previous to HASU opening the stroke unit mainly admitted more local patients.

180 subjects were unable to consent to inclusion in the study within the allocated seven days post stroke diagnosis. A further 150 patients were excluded from the study, for a variety of reasons- including being longer than seven days post stroke, or the researcher not being able to see them in time due to absence. Between July 2009-January 2010 when the study only included first time strokes, 43 stroke patients who had previous stroke were also excluded from the study.

The average age of the excluded subjects was 73 years in age, and the average NIHSS score was 10. These are in line with average nominal data for stroke age and mild impairment following stroke ⁹

Two patients who match the study criteria did not consent to be involved in the study. 125 patients were recruited into the study (100 single incident strokes and 25 subsequent strokes). A breakdown of the problems seen in these patients is summated in Figure 5.3.

Figure 5.3a: Breakdown of Impairments seen in the consented subjects

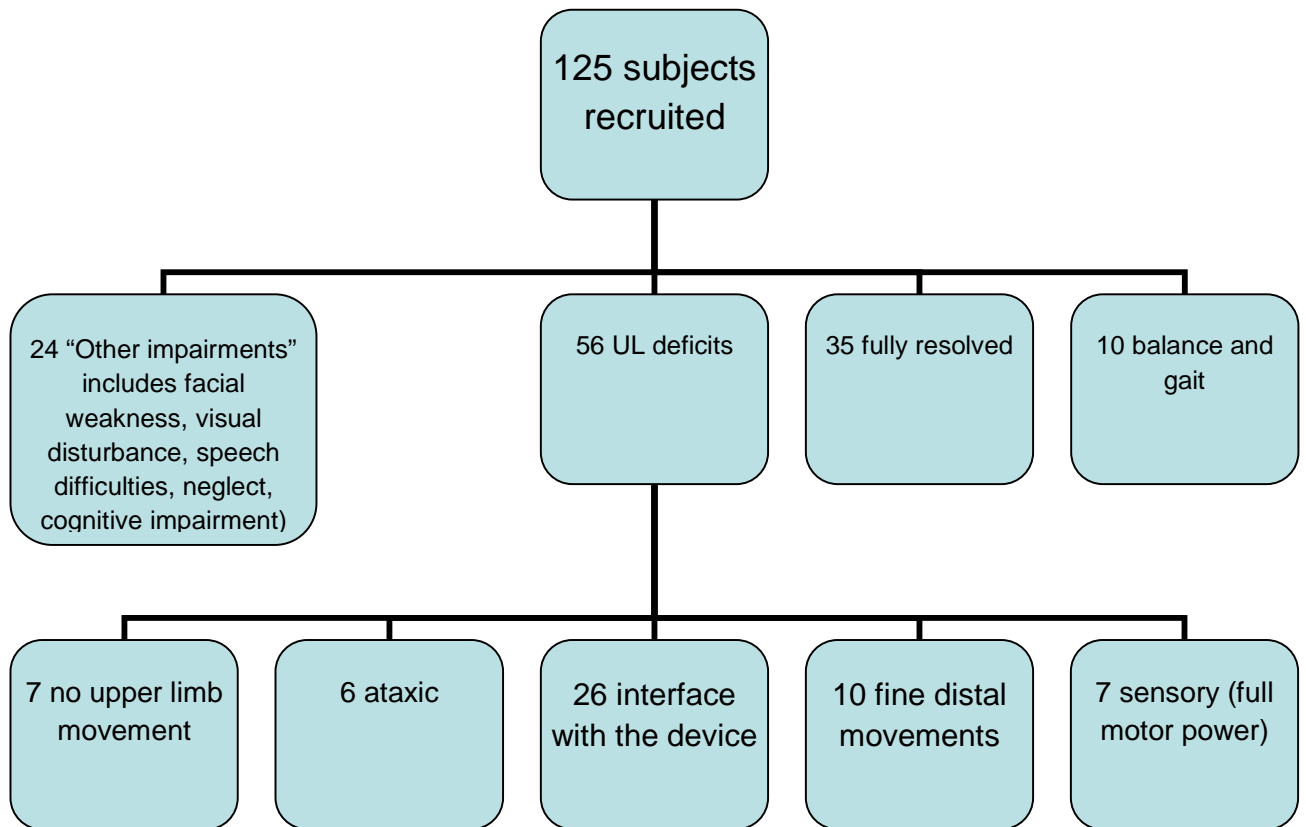
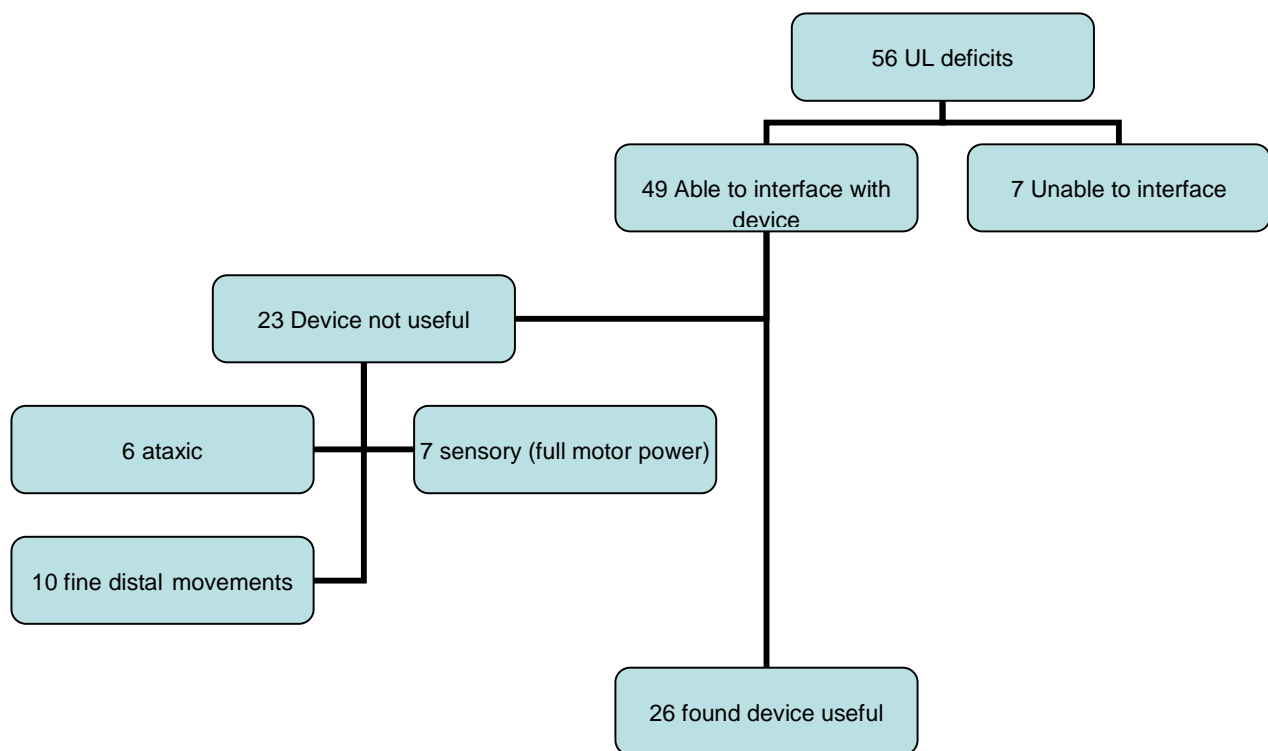


Figure 5.3b: Breakdown of Impairments seen in the consented subjects



Of the 125 participants recruited, 35 subjects on assessment were seen to have fully resolved from the initial symptoms that they presented to hospital with (these participants had been diagnosed with an acute new incident stroke from scan results and clinical diagnosis). Ten of these subjects were found to have no upper limb deficits but difficulties with their balance and gait. Twenty four of the subjects recruited were also seen to have no upper limb deficits but were seen to have other impairments as a result of their stroke, which included facial weakness, visual disturbance, speech difficulties and cognitive difficulties.

Fifty six subjects (45%) did however present with some degree of difficulty using their arm following their stroke. Of the patients with upper limb difficulties, patients with no upper limb movement were unable to interface with the device. Patients with fine distal problems/ ataxic/main problem reduced sensation were able to use the device but it was not sensitive enough to be used as a training aid.(This is shown in figure 5.3 b)

Twenty six of the 56 participants with upper limb deficits were able to interface with pReachMAN (46%). This means that subjects were able to (either independently or with assistance) place their arm on the arm support, rest hand on the hand handle (as shown in figure 5.2) and move the arm support.

Participants with severe arm paresis were able to use this device. Severe paresis in the context of this phase of study was defined as the some flickers of activity in the arm (in the majority of cases, this presented in practice as an ability to shoulder shrug and protract and retract at the shoulder but no other arm movement). Lack of hand movement did not seem to prevent people from resting their arm on the hand handle, because the handle can rest in pronation. People with flickers of shoulder movements were able to use the support to reach with. The most likely mechanism for this is was combination of trunk movement facilitating shoulder extension.

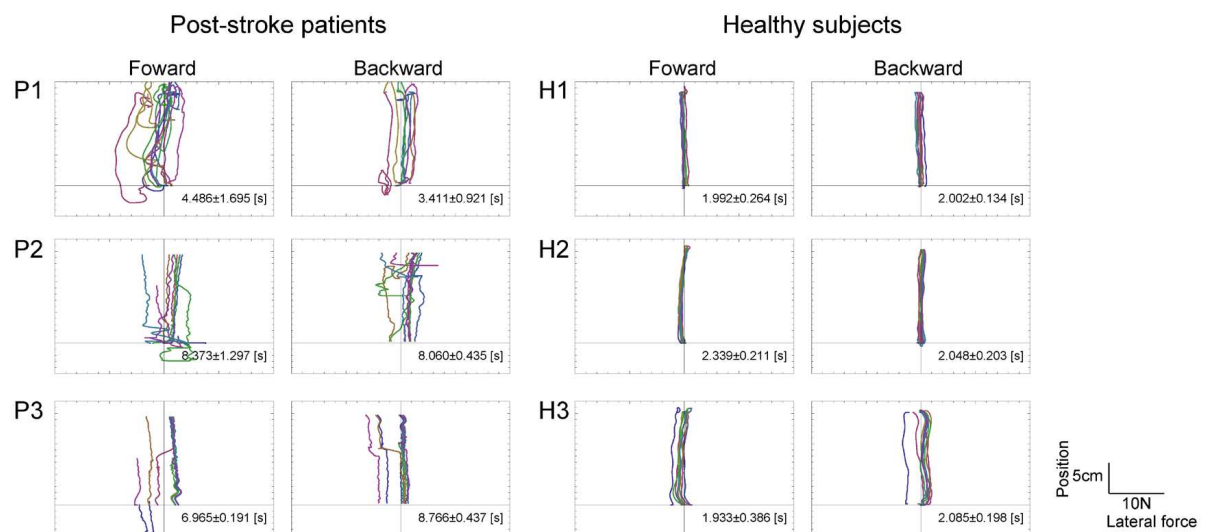
Participants needed to be able to sit out in a chair (which could have supportive back to allow them to sit) for periods longer than ten minutes to be able to use the device. They also needed to be have some level of vision to be able to see the screen. Furthermore participants were required to be able to attend and focus on the task for at least 10 minutes.

It was initially envisaged that weekly data using pReachman could be collected from the subjects who were able to interface with the device. Unfortunately due to the sensors breaking and delays in fixing these this information was not available for all 26 subjects who were able to use the device.

Alejandro Melendez Calderon who designed pReachMAN reports in his PhD thesis on data from three subjects that was able to be processed from the device. He compared this data to three right-handed, healthy subjects (aged between 24 to 29 years old), in order to have a baseline for qualitative evaluation of the order of magnitude of deviations from the patients. He has given permission for this data to be reproduced in this chapter. Further information and analysis from this is available in his Phd thesis.³⁰⁴

Figure 5.4 shows the lateral force applied against the walls of the device versus the hand position along the straight line. Stroke subjects exhibited greater amount of lateral forces and changes in direction than healthy subjects.

Figure 5.4 – Lateral force vs. position along the straight line.



Post-stroke patients performed movements with the paretic arm, while subjects with their non-dominant hand. On the right-lower corner of each figure the mean and standard deviation of the time taken to perform the movements is shown.

All subjects seen at 6 weeks demonstrated improvements in their outcome measures (this was to be expected). This data was used to look at the responsiveness of the outcome measures (and is discussed below in section 5.4.1)

5.4.1 OUTCOME MEASUREMENT SELECTION

The outcome measures that were used in this phase of the study, were analysed to look at the acceptability, targeting and responsiveness of the measures.

Of particular interest was the upper limb scales. Table 5.1. shows the scale range, mean score, skewness and floor/ceiling effects seen in each of the upper limb measure:

Table 5.1.: Data quality, scaling assumptions, acceptability and reliability of the upper limb measures used in the study (N=125)

	<i>FMA</i>	<i>DASH</i>	<i>STREAM</i>	<i>ARAT</i>	<i>ABILHAND</i>	<i>Chedoke</i>
Data quality						
Item missing data %	0	0	0	0	0	0
Computable scale scores %	100	100	100	100	100	100
Acceptability						
Score range	6-100	0-88.3	0-20	57-114	0-100	13-91
Mean score (sd)	80.8 (27)	28.1(28.8)	9.95 (3.11)	93(23)	70.7(33.1)	69.31(26.8)

)				
Floor/ceiling, %	0/47.2	0/27.2	0.8/0.8	20.8/32 .5	8.9/44.4	8.8/44.8
Responsiveness						
Mean score (sd) at 6 weeks	90.3 (30)	20.2 (20)	10.1 (3)	94(25)	79(34)	71(29)

DATA QUALITY

There were no missing data for all the scales and all scales were successfully completed by patients.

ACCEPTABILITY (TARGETING)

This is the targeting of a scale to a sample so that score distributions adequately represent the true distribution of health status in the sample.³⁰⁵ This was achieved by the scores being examined to determine that observed scores were well distributed, mean scores were near the scale mid-point, floor and ceiling effects were low, and skewness statistics ranged from -1 to +1.

This analysis (as shown in Table 5.1.) showed that all the measures observed scores were well distributed. However mean scores for many of the measures (FMA, ARAT, ABILHAND, Chedoke) were not near the mid point of the scale (mostly much nearer to the higher end of the scales). This is also seen in floor and ceiling effects. Ceiling effects were seen in the FMA, ARAT, ABILHAND, and Chedoke measures. Floor effects were also seen with the ARAT. Skewness in the FMA was found to be over the accepted range of -1 to +1.

A possible explanation for the problems seen in targeting of the measures was the high proportion of participants recruited into the study that had no upper limb deficit (55%).

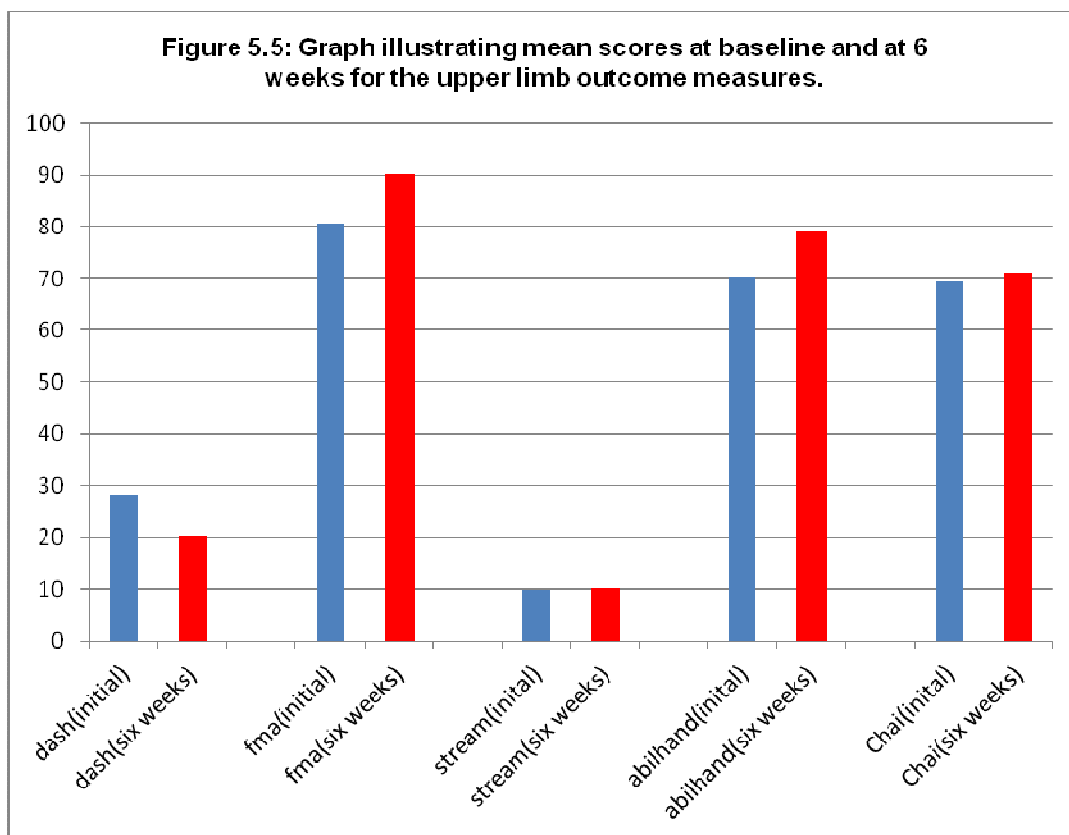
Chapter Four discussed the rationale for scales selected in the studies. Unfortunately upper limb scales have been found to be psychometrically restricted^{258 306} and this was found to be the case in this analysis. Due to the lack of psychometric robust scales in routine use²¹⁴ (as further discussed in Chapter Four) it was decided to continue to use this battery of upper limb measures for the exploratory RCT (which will be described in Chapter 6).

RESPONSIVENESS

Responsiveness is the ability of a tool to accurately detect important changes over time.³⁰⁷ This was evaluated by comparing the mean and standard deviations of the upper limb measures from baseline and at six weeks. This is illustrated in Figure 5.5. All subjects showed improvement at six weeks (which would be expected when looking at subjects early post stroke). However the FMA and Abilhand appeared to show greatness difference in pre and post scores.

The analysis of data quality of the measures suggested that the Abilhand demonstrated the most acceptability, targeting and responsiveness. A further discussion of this is detailed in Chapter Nine.

Figure 5.5: Graph illustrating mean scores at baseline and at six weeks for the upper limb outcome measures.



The time taken to complete the battery of outcome measures varied depending on the severity of participant's upper limb deficit but the maximum it took to complete was thirty minutes and all participants complied with this.

One of the measures, the SF36, was greatly disliked by the majority of participants- with most finding the questions intrusive and many requested not to answer the questions. In particular the first two questions of the measure which ask participants to describe their current health status and how this compared to one year ago were generally disliked. One participant remarked, which describes many of the subject's comments on the measure:

“ I find that an insulting question, how do you think I would describe my health, they have just told me I have had a stroke”.

It was therefore decided to leave out this measure from the RCT.

5.4.2 RECRUITMENT CRITERIA

A number of practical factors presented themselves during the course of this phase of the study which significantly shaped the criteria for the next phase of the study:

Firstly, to be able to interface with the device, patients needed to be able to sit out for a significant length of time (ten minutes or so was found to be a lengthily period for some of the subjects in the very acute phase post stroke), focus and attend to the device to be able to use it. In many cases patients sitting tolerance and attention improved with time.

Therefore, although the study wished to capture acute patients, it was felt to be beneficial to include subjects up to eight weeks post stroke to maximise recruitment numbers.

For the RCT it was envisaged that patients would be able to use the robotic device for 30 minutes or more and therefore a criteria of the RCT was to be able to sit out and attend to the task for 30 minute periods.

The study demonstrated that patients with very little arm movement could use the device (although some arm movement was required). This allowed patients with severely impaired arms to be included in the second phase of the study. This not only allowed a broad recruitment criteria for the second phase of the study but was seen as very encouraging as at present there is little therapy specifically to promote recovery of the severely paretic or paralysed upper limb after stroke.

From the 125 patients that were recruited it was possible to determine recruitment criteria for the next phase of the study (an exploratory RCT using ReachMan robotic device). This was:

1. Acute stroke patients 0-8 weeks since having a stroke
2. Able to consent to treatment
3. Able to understand basic information
4. Able to sit out in a supportive chair if required for at least 30 minutes
5. Able to see the graphics and visual display on the machine
6. Able to attend and focus on the games for at least 30 minutes.
7. Severe to moderate UL impairment. However must demonstrate some degree of arm movement (i.e an ability to shoulder shrug).

5.4.3 RATE AND TIMING OF RECRUITMENT IN PRACTICE

This phase of the study also helped provide a guideline to the rate and timing of recruitment into the next phase of the study. It was felt taking into account the through put of patients from the HASU into local stroke unit (ABIU) to the rehabilitation ward, recruitment numbers were likely to be one to two patients a month into the RCT. Further details of the actual recruitment rates are given in chapter six.

The study also highlighted some important information about recruiting acute strokes into a clinical trial. ULCH trust sees a large number of patients admitted into its stroke unit. However due to the fast turnover of patients (patients only stay in HASU for 72 hours and are then repatriated to their local stroke unit), a large number of patients potentially with upper limb deficits (460) and who may have been able to interface with the device were unable to be assessed or recruited into the study. This was because they were transferred to their local stroke unit (the study had ethics approval for single site recruitment only- UCLH hospitals).

Furthermore, a number of patients were ineligible for inclusion to this phase of the study because they were unable to consent to participation within the seven day time period post stroke (i.e. very early days post stroke). However some of these patients at a later period were notified to the research therapist by the MDT team but were then ineligible for recruitment into the study.

5.5 CRITIQUE OF THE METHODOLOGY USED IN THIS RECRUITMENT STUDY

The aim of this study was to define the number of people who would be able to use the device in practice, and define recruitment criteria. These aims were met, however there were limitations with this phase of the study.

The people recruited to the trial represented a heterogeneous population, including those with both haemorrhagic strokes and infarcts, single incident strokes as well as people who had had multiple strokes. Although this mirrors the population treated in clinical practice, the research design could be criticised for including people with haemorrhage as this type of stroke has a different aetiology and, sometimes prognosis, from infarcts that comprise

the majority of strokes. Furthermore prognosis and rate of recovery can also differ with subsequent stroke.¹⁶

The study was not blinded and the Research Therapist completed the measures with the participants and this could have introduced bias.

There were various absences of the Research Therapist during the trial period. Furthermore, the Research Therapist did not work over the weekend. Stroke patients admitted to the Trust during these time periods who may have been eligible for inclusion to the study, were unable to be seen or known to the researcher. Therefore the data presented here cannot be verified as being an accurate representation of the number of strokes admitted to UCLH during the time period or necessarily reflects completely consecutive patients that were admitted into the Trust.

This phase of the study aimed to look at the proportion of acute participants who could potential use a robotic device. For this reason every person who had had a stroke in UCLH over the time period were invited to participate in the study. This did however mean that a proportion of participants were recruited that did not have upper limb deficits. This resulted in some problems when analysing the targeting of the outcome measures.

5.6 SUMMARY

This chapter has reported the findings of a recruitment study that was performed to establish the proportion of acute stroke patients that could potentially benefit from rehabilitation using a robotic device. Clinical trials that have investigated the use of robotic as an adjunct to upper limb rehabilitation, have used a variety of impairment levels and little work has looked at the use of these devices in the early, acute phase following stroke (this has been discussed in Chapter Two). However in clinical practice it is important to know the amount and impairment level of patients who could potentially use these devices. This phase of the study provided useful information about the rate and timing of recruitment in practice, the recruitment criteria for an exploratory RCT and analysis whether the battery of outcome measures selected were practical, feasible and appropriate.

The next chapter will describe the exploratory RCT that was performed which build on the information established in this study.

CHAPTER 6- AN EXPLORATORY RANDOMISED CONTROL TRIAL TO EXPLORE
THE EFFECT OF THE USE OF A ROBOTIC DEVICE ON UPPER LIMB ACTIVITY
IN SUB ACUTE STROKE PATIENTS.

6.0 INTRODUCTION

Chapter Five described the process of defining a recruitment criteria & the identification of the proportion of patients who could participate in robotic training using the Reachman robotic device. Using this information an exploratory Randomised Control Trial was carried out. This chapter will discuss this exploratory trial. This feasibility study allowed variations of the intervention to be tested and formed a Phase II study using the MRC framework. Phase II of the framework facilitates both quantitative and qualitative designs being used. This chapter will report how all the quantitative data was collected and will discuss the results. The following chapter will discuss the qualitative data collected through semi-structured interviews at the end of the period of intervention.

This Chapter will describe an exploratory RCT that was carried out to investigate the effects of using ReachMAN robotic device on arm movement and function in the sub-acute phase after stroke.

Chapter 2 has discussed the literature that suggests robotic therapy may be a useful adjunct to assist in upper limb recovery and that it may allow greater improvement with this when compared with “conventional therapy”. This has been particularly seen when used in acute or the subacute stroke population. There has however been a paucity of research trials that have looked at robotic therapy in the acute stroke population. Theoretically, the acute phase post stroke is when potential for significant functional gain is greater. Therefore further research looking at robotic devices in the early stages post stroke is needed. The study detailed below aimed to fill this research gap.

6.1 OBJECTIVES

6.1.1 HYPOTHESIS

In this study the hypothesis tested was that an early use of a robotic aid (Reachman) in addition to conventional therapy following stroke would improve arm movement more than therapy alone.

6.1.2 NULL HYPOTHESIS

The null hypothesis was that there would be no difference between the groups as measured by the Fugl Meyer Upper limb Score and other secondary outcome measures as a result of the intervention- using a robotic device.

6.2 AIMS

The aims were to investigate:

- i. The resource needs in terms of engineering, trained and untrained rehabilitation staff to bring robotic training into routine practice
- ii. The frequency, duration and intensity of robotic training tolerated by patients
- iii. The increase in practice time that this represents
- iv. The size of a definitive randomized control trial.

6.2.1 RESEARCH QUESTIONS

1. What are the effects of using a robot on the motor performance of the hemiplegic upper limb in the sub-acute phase after stroke?
2. What severity of arm impairments could use the device and is there a difference in the potential benefit of the aid depending on the severity of arm paresis?

6.3 METHODOLOGY

An RCT involves the random allocation of participants between an experimental group whose members receive the treatment or intervention and control group who receive standard treatment. The outcome of the groups is then compared.

This methodology was chosen for this part of study because as the literature reviewed in Chapter Two demonstrated the use of robotic devices has been extensively examined in studies with no comparator group. Therefore, further work using this methodological design was not felt to be warranted. However, there has been limited work comparing upper limb recovery in the subacute phase with rehabilitation alone with additional use of a robotic aid. Therefore an RCT design was felt to be appropriate.

There are different types of Randomized control trials: Cluster RCT and cross over RCT. For most trials the unit of randomization is the individual person being allocated to a specific intervention or to a control or placebo. There is a growing interest in the use of cluster randomization in community trials. Cluster randomized trials are trials that individuals are not randomized but units (clusters) such as clinics, hospitals, physicians or families. Advantages of cluster randomization trials are that they reduce “contamination” of the interventions between groups, they can increase participation, and they allow for better administrative and logistic organisation in implementing the intervention. The MRC guidelines discuss using cluster randomization in complex interventions²³⁸. However for this study a cluster randomized trial was not chosen as the study design. This was due to the small nature of the trial (it being a feasibility study) which was based in one trial center.

A crossover design was considered for the study. This is using within patient comparison (i.e. participant acts as own control). For example both the intervention and the control group would use the robotic device, this would just be randomized to different time periods. This design was trialed in a pilot study performed on three subjects subsequent to the RCT (This is reported in Yeong et al (2010)²⁴⁴. Unfortunately however this was not found to be practical to implement in practice. The intervention period for the groups was six weeks, and not all subjects stayed as inpatients for the whole 12 week period needed for a cross over design (i.e. 6 weeks control group/ usual rehabilitation, Six weeks use of the robot). Therefore a conventional RCT design was used.

Poorly designed and reported RCT trials are common in the literature and to combat this problem the Consolidated Standards of Reporting Trials (CONSORT) statement³⁰⁸ was written and first published in 1996 and updated in 2001 and 2010³⁰⁹. These guidelines are used to structure this chapter. Within these guidelines the following need to be considered:

SAMPLE SIZE

The sample size for a trial needs to be considered carefully as ideally it needs to be large enough to have a high probability (power) of detecting a statistically and clinically difference if such a difference exists³⁰⁹. An aim of this study was to provide details for a power calculation of sample size for a definitive RCT.

RANDOMISATION

Participants should be assigned to comparison groups in a trial on the basis of a chance (random) process characterised by unpredictability³⁰⁹. Random allocation between experimental and control groups means that study participants were allocated to the groups in such a way that each has an equal chance of being allocated to either group. The purpose of random allocation is to achieve similarity of baseline characteristics in the treatment groups. If the treatment groups differ in baseline characteristics, confounding may result. Confounding factors are those that influence treatment and outcome measures and include demographic characteristics, prognostic factors, and other characteristics that may influence someone's likelihood of participating in or withdrawing from a trial. Therefore, any differences between treatment groups in outcomes may not be due to differences in the treatment received but to differences in baseline characteristics. Pure randomisation is based on a single allocation ratio is known as simple randomisation (a 1:1 allocation ratio analogous to a coin toss).

Block randomisation is randomising participants within blocks such that an equal number are assigned to each treatment. This type of randomisation can be used in trials with small numbers to assist with an even distribution among groups.

Block randomisation with blocks of size four was used in this trial (further details of this are given in section 6.5) to allocate patients to treatment group. This involved selecting groups of four consecutive patients recruited into the study. Within each group of four patients, two were allocated to the control group and two to the treatment group. However, the order in which treatments were allocated in each block was random. This type of randomisation was used to ensure that consecutive patients were distributed equally between treatment groups.

ALLOCATION CONCEALMENT

The method used to implement random allocation is called allocation concealment which seeks to prevent selection bias, protects the assignment sequence until allocation, and can always be implemented³⁰⁹.

BLINDING

Blinding refers to withholding information about the assigned intervention from people involved in the trial who may potentially be influenced by this knowledge. It seeks to prevent performance and ascertainment bias, protects the assignment sequence after allocation, and cannot always be implemented³⁰⁹. Unfortunately this feasibility study did not use blinding. This will be further discussed in Chapter Nine.

LIMITATIONS WITH RCT DESIGN

There are problems with using RCTs in therapy intervention trials. RCTs predominately identify changes that are statistically significant, this may miss however the clinical importance of change, , ³¹⁰. Furthermore considering a treatment technique in relation to a heterogeneous population (e.g. stroke) is challenging as people may respond differently to the intervention, and an RCT design does not always reflect individual change.

It is also difficult to perform “gold standard”, high quality randomised control trials when researching neuro rehabilitation ³¹¹. It is extremely hard to perform double blinded research , a placebo treatment unknown for both the therapist and the patient, unless there is a drug or injection treatment, as both will usually be aware of the treatment Kersten et al (2010) ³¹¹ further discuss the difficulties in performing RCT in neurological rehabilitation research, especially due to the complexity of rehabilitation interventions, selective research samples and multiple understandings of perspectives of benefits.

The MRC framework acknowledges the difficulties with complex interventions and the framework process provide a guide to assist with performing RCT having considered these issues. The feasibility RCT study described in this study and the qualitative study described in Chapter Seven follow these guidelines, aiming to address some of the unanswered questions in the robotic literature and assist with the development of a definitive RCT, acknowledging the difficulties in performing gold standard RCT research in this area.

6.3.1 TRIAL DESIGN

The trial was randomised and controlled with two comparator groups. The trial was a single centre study. Measurements were taken pre- and post intervention.

6.3.2 PARTICIPANTS

Patients within 0-8 weeks of stroke with upper limb impairment who matched the inclusion criteria were approached for recruitment into the study. Inclusion and exclusion criteria have been discussed in Chapter 5. The eligibility criteria for the trial were:

1. Acute stroke patients 0-8 weeks since having a stroke
2. Able to consent to treatment
3. Able to understand basic information
4. Able to sit out in a supportive chair if required for at least 30 minutes
5. Able to see the graphics and visual display on the machine
6. Able to attend and focus on the games for at least 30 minutes.
7. Severe to moderate UL impairment. However must demonstrate some degree of arm movement (i.e an ability to shoulder shrug).

6.3.3 STUDY SETTING

The study took place at the National Hospital for Neurology and Neurosurgery (NHNN) from January 2010 through to March 2011. The trial recruited patients from University College London Hospitals (UCLH) stroke services

UCLH is one of the leading centres for stroke research. Stroke patients are first admitted into a hyper acute stroke unit (1643 approximately per annum). Within 72 hours patients are transferred to their local stroke unit. More than 400 patients with stroke are admitted to the NHNN each year. The NHNN houses the Acute Brain Injury Unit where local Camden and Islington patients following stroke are admitted. From this unit, patients who require rehabilitation are assessed and admitted to National Rehabilitation Unit (NRU) where they on average receive three months rehabilitation. The NRU is an 18 bedded specialist rehabilitation unit, in 2010 23.2 % of people admitted to the unit had had strokes. The NHNN also includes the Albany Rehabilitation Unit which provides rehabilitation for stroke patients who live in Kensington & Chelsea or Westminster PCT. This is a 10 bedded unit. In 2010 74.2% of patients admitted to this unit had a diagnosis of stroke.

6.3.4 ETHICS

Ethical approval for this stage of the study was obtained from the joint research ethics committee of the NHNN and the ION (see Appendix V). The trial was sponsored by University College London Hospital Trust, and funded by a project grant from The Stroke Association. (Approval number: 08/H0716/13. Project Grant: TSA 2007/14). All participants gave their informed written consent.

6.3.5 STUDY INFORMATION

The information sheet for participants was written using UCLH guidelines; this sheet gave them further information about the study, possible interventions and how the data collected would be used (see Appendix VI). Each participant read the information sheet prior to agreeing to participate in the service. Once verbal agreement was reached a consent form was then signed. (see Appendix VI).

6.3.6 PROCEDURE

Screening was undertaken by the Research Therapist. Ward lists were reviewed on a regular basis, the MDTs were consulted regarding the suitability of people for the trial, and medical notes were screened for all those the MDT considered suitable for the trial. On a weekly base the Research Therapist would contact the relevant wards (Acute Brain Injury Unit, NRU and ARU) to discuss if they had been any new admissions that may be suitable for the trial. Wherever possible, the Research Therapist was introduced to potential participants by a member of the MDT. A verbal explanation of the trial was given to the individual (and also to their relatives and friends, when they were present). This was supported by the provision of the Patient Information leaflet. Individuals were encouraged to discuss their participation with family/friends/members of the MDT, and to ask questions about the trial. It was stressed that the individual could withdraw from the trial at any stage and that participating would not affect their usual care. If there was any doubt the participant was excluded from the trial. The Research Therapists, family and friends of the individual, and the Speech and Language Therapists supported people with aphasia in the consent process. All prospective participants were given at least 24 hours to consider taking part in the trial before written informed consent was sought. Informed consent was

taken by the Research Therapist, a copy of the consent was given to the individual and a copy was placed in their medical records.

Baseline measures (detailed in section 6.5) were made on Day One by the Research Therapist. A standardised position was used (i.e. sitting upright at a table) for the clinical scales; however, when this was not possible (e.g. due to lack of assistance with transfers or the severity of impairment), the best possible position was adopted and noted in the trial records. All participants were given the opportunity to complete the patient reported measures in their own time (but within 48hours of recruitment into the trial). If subjects and their family requested assistance with the PROM, it was administered face-to-face by the Research Therapist.

On the following day (Day Two) the participant was randomised into one of the two groups. Each day the participants were checked for adverse events.. If adverse effects, which could not be explained by a clinical reason other than participation in the trial, were experienced on three consecutive days during the treatment period then treatment was to have been discontinued, however, the outcome measurement battery was completed. Outcome measures were collected at six weeks.

6.4 INTERVENTION

6.4.1 CONTROL GROUP

Participants in the control group received their usual practice rehabilitation which consisted of a minimum of two 45 minute treatment session each day from physiotherapy and occupational therapy. Therapy sessions were conducted in either the rehabilitation gym, by the patient bedside or in other therapy areas in the rehabilitation units. In addition patients had input from speech and language therapy, psychology, and social work as required and practice/exercise sessions supervised by nurses and rehabilitation assistants. The input all patients receive were recorded through integrated care pathways and the Northwick Park Therapy Dependency Scale and the Northwick Park Nursing Dependency Scale This constituted usual practice at the NHNN and enabled recording of the amount of therapy patients were receiving. As well as these scales, the amount and content of therapy given to participants during the intervention phase of this trial was

documented using a treatment schedule. This treatment schedule has been tested for its reliability and has been used to record physiotherapy in a trial of functional upper limb strength training.^{159;312}

6.4.2 EXPERIMENTAL INTERVENTION

The intervention group received usual practice rehabilitation (as described for the control group) and participated in repetitive training using the robotic device.

ReachMan was located in the rehabilitation gym .

The use of ReachMAN intervention had three distinct phases

1. *Initiation of practice.* The physiotherapist and engineer (Mr Che-Fai Yeong) worked with the patient to establish an appropriate physical set-up and task demand for the patient. They prepared a schedule and instructions that formed the basis of regular practice.
2. *Establishing practice.* The physiotherapist then worked with a rehabilitation assistant to set up the patient each time the patient wishes to practice, checking that the schedule clearly described how to set up both device and patient.
3. *Maintaining practice.* The rehabilitation assistant set up the device with patient when requested.

Intervention quality was monitored on a weekly basis by the physiotherapist.

The experimental invention had to fit around routine care and not interfere with therapy sessions, ward rounds, meal times, or medical investigations. In addition, when participants were using the ReachMAN device their experience of fatigue, their preferences for timing of using the device and the visits of their family and friends were taken into consideration. All these factors could potentially reduce the amount of time the subjects spent on the device. Consequently, the research therapist paid particular attention to communication with clinical staff and participants regarding the flexible timing of intervention.

The aim was that subjects would have a maximum of 30 (5 week days over six weeks) half-hour robotic therapy sessions during the intervention period, but less if they were discharged earlier than six weeks.

During the robot rehabilitation session, the subject sat comfortably on a wheelchair or on a standard chair while the impaired hand was rested on the arm support. The height and distance of the robot were adjusted such that the elbow was flexed at 90° , shoulder abduction at about 35° and shoulder flexion at 0° (all with a 10° tolerance). The hand grasped the robot handle and was secured with Velcro band. The sequence and number of sets were adapted to the performance of the subject, but all subjects started with the reaching exercise followed by pronosupination, grasping, then the combination of pronosupination and reaching. Each sets contained 10 trials, and maximally 10 sets were completed for each exercise. However, if there was no movement at all, the particular exercise was limited to three sets. The first session was for the subjects to familiarize with the robot. Subjects could try the exercise modules freely without having their performance assessed. During the second and last sessions, subjects were assessed with the robot on all four exercise modules, using a standard difficulty level (Seven.) From the third session onwards, each subject progressed from lowest level of difficulty on each of the exercises. Subjects could progress of maximally one level up on each day, if their score was over 90% with 10 hits thrice in a row.

ReachMan was programmed with eight difficulty levels (one the easiest up to eight the hardest). Each level had an increased range of motion and resistance to the movement. . At the lower levels participants were only required to put in relatively little effort to move. For example, only 2N was required to trigger the reaching movement, 0.05Nm for the pronosupination and about 1N for grasping. However, in contrast level 8 required higher forces to trigger a movement, about 5N for reaching movement and 0.15Nm for pronosupination.

The protocol followed for the intervention phase can be found in Appendix II . This was devised following piloting of the intervention in three subjects. This pilot has been reported in Yeong et al²⁴⁴.

6.4.3 TRUNK RESTRAINT

A modified form of trunk restraint was used with all participants when using the device (A photograph of this is shown in Photograph 6.1). Studies that have investigated normal reach to grasp pattern have found that stroke patients use compensatory trunk movements when reaching for an object within reach (as compared with normal controls who only use a trunk strategy when objects are placed beyond their reach).¹²³ Trunk restraint (this is where the subject trunk movements are limited by a strap or belt) has been shown to result in an immediate improvement in active range of movement and inter-joint co-ordination in moderately to severely affected stroke subjects.⁴⁹

Most trials using robotic devices use some form of trunk restraint (ie a harness attached to the patient) ^{108;182}(In the case of the MiTManus device this is in the form of a 3 point seat belt,¹⁹³ or two shoulder and a waist belt seat belts which limit trunk movement.)

The use of the non- assistive interface (p ReachMAN as described in Chapter 5) showed that subjects used compensatory trunk movements when using the device. Therefore to maximise arm movements alone a form of modified trunk restraint was used with all subjects who used ReachMan. A summary of this procedure with instructions as to how this was practically achieved can be found in Appendix II

Photograph 6.1-Trunk Restraint used in the study.



6.5. OUTCOME MEASURES

Chapter Four has described in detail the scale selection strategy used and selection of scales. Chapter Five has then discussed how these scales were tested for appropriateness and reasons why some scales were not used in this exploratory trial. The study therefore used the following outcome measures: STREAM, CAHAI, ABILHAND, FMA, ARAT, EQ5D, Barthel Index, NIHSS and DASH

In addition to the scales used in Phase One, one additional scale was used in this phase of the study: the Ashworth score³¹³. The Ashworth score was used in the study as it was felt it would be useful to record any increased tone participants had on baseline and whether this changed with the treatment interventions. The score is the most popular and consistently used clinical measure of spasticity.³¹⁴ The most common version used of this scale in regards to the upper limb is the modified version, and this was the version used in this study.

The modified Ashworth score is a five point scale :

- 0 No increase in muscle tone
- 1 Slight increase in muscle tone, manifested by a catch and release or by minimal resistance at the end of the range of motion when the affected part(s) is moved in flexion or extension
- 1+ Slight increase in muscle tone, manifested by a catch, followed by minimal resistance throughout the remainder (less than half) of the ROM
- 2 More marked increase in muscle tone through most of the ROM, but affected part(s) easily moved
- 3 Considerable increase in muscle tone, passive movement difficult
- 4 Affected part(s) rigid in flexion or extension

Other studies looking at robotic intervention have used this scale to look at increased tone in the upper limb with this use of a robotic device.²⁰⁰ Tests of inter and intra-rater reliability have had conflicting results and the scale is unable to distinguish between the reflex and non-reflex components of increased tone. Despite the limitations with this measure, due to the ease of competition, and repeatability with other studies it was chosen for use in the exploratory trial.

6.5.1 MEASUREMENT BATTERY

Measurement points were at baseline before randomization and at 6 weeks. In addition, assessment for adverse events was conducted on each working day of the study period.

6.5.2 SAMPLE SIZE

The study aimed to recruit 20 subjects in each arm. This was a pragmatic recruitment figure, based on the length of time proposed for the trial to be carried out and the recruitment data gathered from phase 1 of the study (detailed in Chapter 5) In total 37 subjects were recruited to the study.

6.6 RANDOMISATION

Section 6.3 discussed different methods of randomisation. Block randomisation with blocks of size four was used in this trial to allocate patients to treatment group. This involved selecting groups of four consecutive patients recruited into the study. Within each group of four patients, two were allocated to the control group and two to the treatment group. However, the order in which treatments were allocated in each block was random. This type of randomisation was used due to the small sample size to ensure that consecutive patients were distributed equally between treatment groups.

Furthermore, this type of randomization was chosen to maximise access to the ReachMan device, as treating four patients simultaneously on the machine would not have been possible. Following consent and the completion of baseline measures, the participant was given the next available place on the Excel spreadsheet that had a random group allocation. This allocated them to either control (B) or treatment group (A). The string was blocked in groups of 4 (see example below). A computerised randomisation programme, had previously determined the randomisation order. (There were six possible permutations of allocation: AABB, ABAB, ABBA, BABA, BAAB, and BBAA and the computer generated these blocks of permutations randomly for all of the recruited subjects).

Table 6.1: Example of the block randomisation used in the study.

Subject code	Group: (A=Treatment B=Control)
AH001	A
JB105	A
ER003	B
JS102	B
MG104	B
CF105	B
AW001	A
MS106	A

6.7 STATISTICAL METHODS/ ANALYSIS

Baseline characteristics were compared between the randomised groups to check for approximate balance in patient characteristics. All analyses were carried out on an intention to treat basis.

Advice was taken from, Pauline Rogers statistician (UCL), to facilitate the data analysis at this stage. Due to the low numbers and therefore data not being normally distributed non-parametric tests were used to analyse the data. The Wilcoxon signed-rank test was used. The Wilcoxon signed-rank test is a non-parametric statistical hypothesis test used when comparing two related samples, matched samples, or repeated measurements on a single sample to assess whether their population mean ranks differ (i.e. it is a paired difference test). It can be used as an alternative to the paired Student's t-test, t-test for matched

pairs, or the t-test for dependent samples when the population cannot be assumed to be normally distributed. Wilcoxon rank-sum test is a non-parametric statistical hypothesis test for assessing whether one of two samples of independent observations tends to have larger values than the other. It is one of the most well-known non-parametric significance tests.

Results from analyses of the secondary outcomes were interpreted cautiously and considered as hypothesis generating rather than providing conclusive results.

6.8 RESULTS

6.8.1 RECRUITMENT

Recruitment to the trial commenced in January 2010 and continued until March 2011. Following a nine month break (due to researcher going on maternity leave), the trial recommenced in December 2011 for five months. 14% of those admitted with a stroke to either the acute brain injury unit or two rehabilitation units and who were screened for eligibility was recruited to the trial. The main reasons for not meeting the eligibility criteria were unable to follow commands (27%); transfer to other hospital for rehabilitation (39.6%); unable to sit out for 30 minute period (17%). Of those eligible, 1% refused to participate (2 patients)

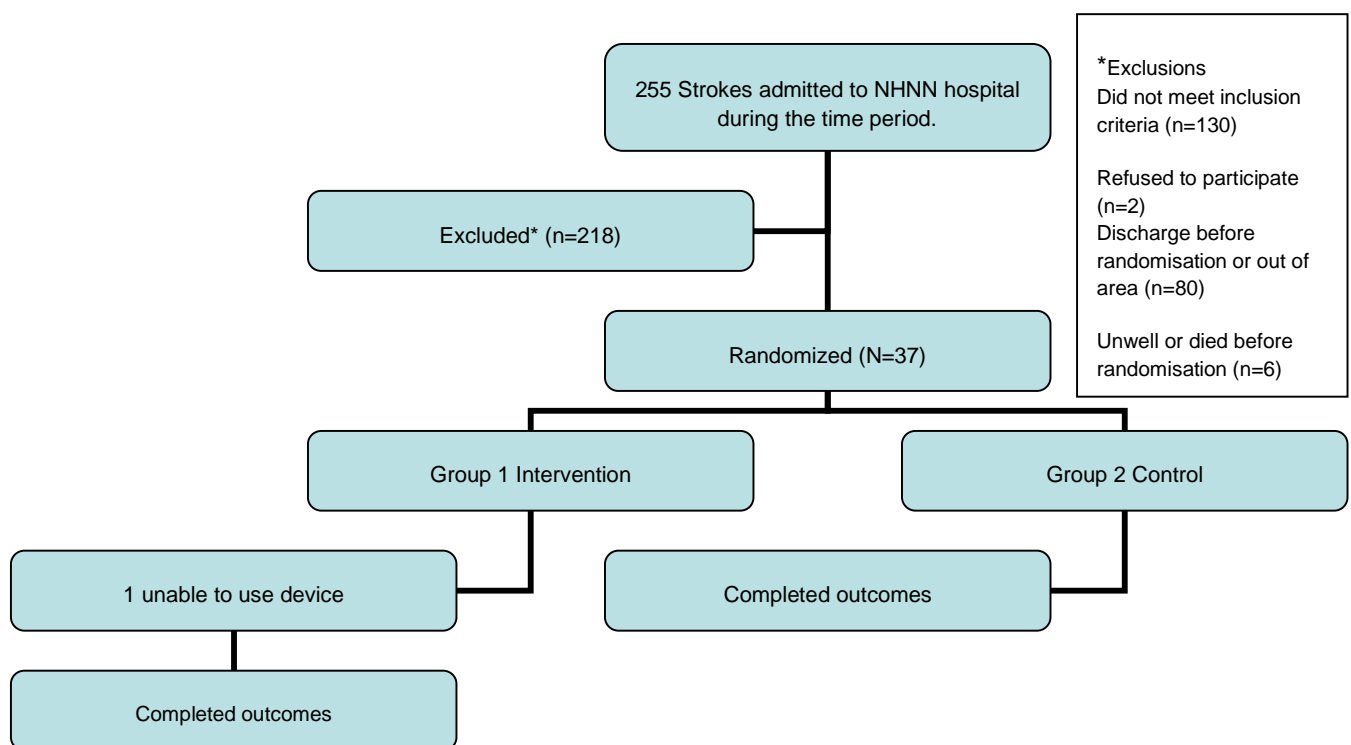
Specific problems regarding recruitment related to a high proportion of potential participants from out of area and transferring to other hospitals for rehabilitation. Cover for the Research Therapist was not available, and breaks in screening and recruitment were therefore required to allow for staff holidays. This did impact on recruitment to the trial. Furthermore no cover was available when the Research Therapist went on maternity leave and this meant an extension of the study recruitment period and potentially lost subjects.

6.8.2 PARTICIPANT FLOW

All participants recruited to the control group completed the trial. One subject recruited to the intervention group ceased using the robot after a week as he was unable to use the device. This subject had arm apraxia and on reflection he should have been excluded from the study on the basis of this. It was however possible to complete the outcome measures

for this participant and so his results are included in the analysis. Another patient complained of shoulder pain after four weeks of using the device, he therefore discontinued to the use device (this will be discussed in more detail in adverse reactions below). It was also possible to complete measures on this participant and his results were also included in the analysis. A summary of the flow of participants through the trial is given in Figure 6.1

Figure 6.1: Flow of participants through the trial (CONSORT diagram)



6.8.3 BASELINE DATA

The baseline characteristics for the participants in the trial are given in Table 5.3 (below). In total, 37 participants were recruited to the trial. Both groups had equal numbers of females (8), the robot group had one extra male subject (11) than the control group (10). The age profile of the participants is illustrated in the histogram below (Figure 6.2). The youngest participants were 25 years old, and the oldest was 85, giving a range of 60 years. The ages of the participants deviated from a normally distributed curve, with peaks

in the younger age group and a peak between 75 and 85 years of age. The older group is in accordance with the increased incidence of stroke with older age. The younger peak is not explained by stroke incidence but may be site specific (this will be further discussed in the discussion and Chapter Nine). The ages were however evenly matched between the treatment and control groups.

There was no significant differences between the groups at baseline on any of the measures.

Figure 6.2: Histogram showing the age profile of participants in the study.

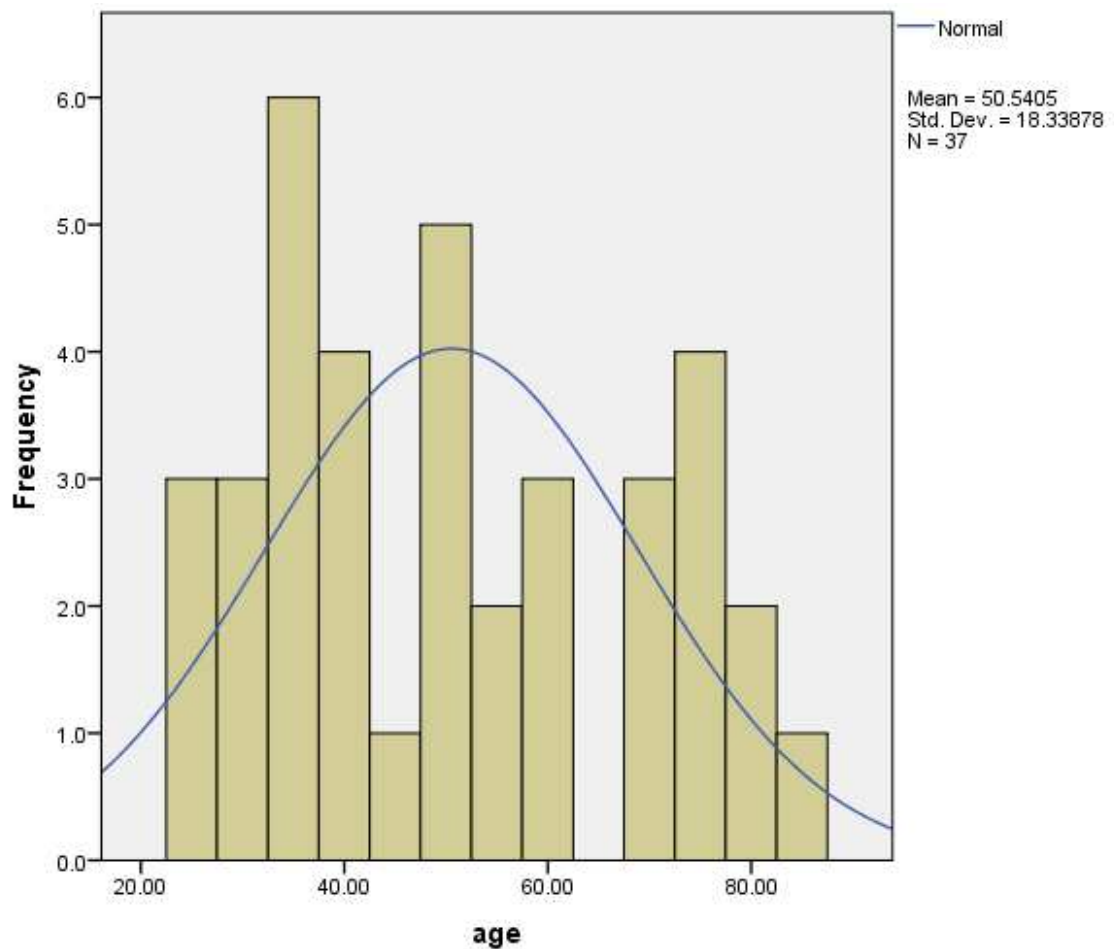


Table 6.2: Baseline characteristics by allocated group

	Treatment	Control
Age Mean (range) (SD)	53 (25-78) (19.31)	47(25-85) (17.32)
Sex – female	44%	44%
Weeks since stroke(range)	5.4 weeks (1-8weeks)	5.2 weeks (1-8 weeks)
Type of stroke:		
Ischemic	65%	65%
ICH	35%	35%
Side Affected :		
Right	47%	52%
Left	52%	47%
Dominant side (Y)	35%	41%
FMA UL Mean(Range) Median (IQR)	19(5-51) 18 19	19(5-54) 20 20
NIHSS (baseline) Range Median (IQR)	4-15 9 6	5-15 10 5.25

65% of participants in both groups had suffered an ischemic event as opposed to the lower number of subjects who had suffered a haemorrhagic stroke (35%). This represents a slightly higher number of haemorrhagic strokes than the normal (where appropriately 15-20% strokes are haemorrhagic in nature³¹⁵). Regarding recovery, it is generally believed that hemorrhagic stroke survivors have better neurological and functional prognoses than non hemorrhagic stroke survivors³¹⁵. Therefore the higher than normal levels of haemorrhagic strokes may influence the results seen. However as these were evenly matched in both groups this should not significantly influence the results.

6.8.4 COMPARISON OF THE BASELINE CHARACTERISTICS OF THE GROUPS

The groups were evenly matched in terms of the total number of participants, age, gender, type of stroke, hemisphere and hand dominance.

Mean time since stroke ranged from one week till eight weeks and the time period since stroke was evenly matched between both groups. As these ranges fall within the sub-acute period it is likely that the potential for recovery would be similar in each of the groups. It was hoped to recruit more subjects very early post stroke, but most subjects (as seen by the mean) were recruited at five to six weeks post stroke.

The median baseline score for the FMA was slightly lower in the robotic group. The inter-quartile ranges of the baseline scores were however very similar across the two groups. Severity of motor impairment early after stroke is thought to be an important prognostic indicator of motor recovery ³¹⁶, so this could have impacted the results.

ADVERSE EVENTS AND WITHDRAWALS

Only one participant experienced an adverse event (pain over three consecutive days) during the study, during his fourth week of using the device. The study protocol stated that participants should be withdrawn from the intervention if there was no cause other than the treatment for the pain. The MDT monitored the participant very closely and advised that they considered the subjects pain was not due to the use of the robotic device. However the participant considered that the use of the robotic device was exacerbating his pain (this is also seen when he was interviewed – described in Chapter 7), and in adherence to

study protocol guidelines, it was therefore decided the subject should stop using the robotic device, and the intervention was ceased after four weeks.

Another participant was withdrawn from using the robot as he was unable to follow the program. This participant presented with arm apraxia and it was felt this impeded on his ability to use the device. In hind sight he probably should have been excluded from the study. The results of these two participants have been included in all of the analyses.

ANALYSIS OF THE INTERVENTION

A total of 475 (out of a potential 570) treatment sessions were completed by all participants using the robotic device. A number of sessions were missed due to the device breaking down and requiring support to get the device working again. Very few treatments were missed at the participants' request. Therapy and other ward commitments affected a large number of treatment sessions. A number of sessions were missed due to the Research Therapists' or Rehabilitation Assistants other commitments or absences.

Table 6.3: Reasons for missed or shortened treatments

Reasons for missed treatments (where details available)	
Reason	Missed treatment
Participant request	1
Participant unavailable (e.g. visitors)	8
Participant unwell	10
Physiotherapy	5
Speech and Language Therapy	3
Occupational Therapy	4
Other ward activities (e.g. ward round, wash)	34

Therapist/RA unavailable	14
Device not working	16

6.8.5 NUMBER OF TRIALS AND MOVEMENTS PERFORMED BY THE PARTICIPANTS ON THE ROBOTIC DEVICE

The research team engineering partners at Imperial University are currently analysing the data stored on ReachMAN computer. However a preliminary analysis suggests participants performed 300 trials.

On average participants spent 20 minutes on the device. Most expressed fatigue and that this was most time they could do on the robot (this is discussed further in Chapter Seven).

6.8.6 ANALYSIS OF CONVENTIONAL PHYSIOTHERAPY

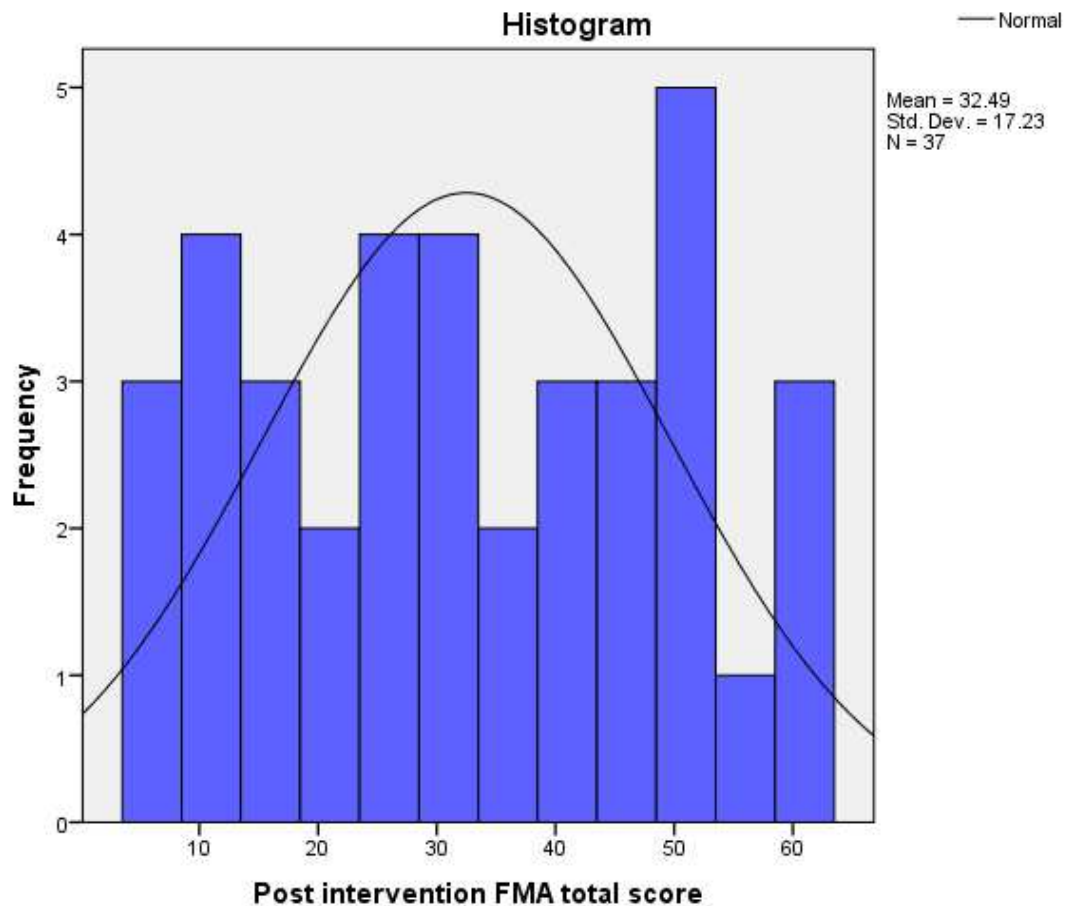
The outcome of the trial may have been influenced by the conventional physiotherapy and occupational therapy received by the participants. Recording forms were therefore given to the therapists in each unit with a request that they were completed for the six weeks of the trial. It had been hoped to include an analysis of the conventional therapy received. Unfortunately, very few of these forms were completed. The integrated care pathway and Northwick Park Therapy Dependency Scores forms showed that each subject received on average 45 minutes of physiotherapy a day. However how much of this was spent on upper limb therapy is unfortunately unable to be analysed.

6.8.7 OUTCOME MEASURES

FUGL MEYER UPPER LIMB ASSESSMENT

The primary outcome was the FMA. A histogram of the frequency of the outcome scores on the FMA across all groups was drawn to assess the distribution of the results (Figure 5.10 below). The results did not follow a normally distributed pattern and confirmed that non-parametric statistics should be used to analyse the data.

Figure 6.3 Histogram demonstrating frequency of outcome score on the FMA across all groups



The Wilcoxon rank –sum test was applied to the data. No significant difference was found between control and Reachman population at the start of study (Wilcoxon rank-sum test $p=0.685$). Significant change in pre and post scores of both control and Reachman was seen with a Wilcoxon signed-rank test ($p=0.0001$) in both cases. This shows that all subjects had improved arm movements following six weeks of treatment. However no statistically significant change was seen between the control and the intervention group ($p=0.210$). Greater improvements for subjects who used Reachman however were seen. The standard deviation of difference between pre and post results of ReachMan were two times higher than the pre-post difference in control group. (Control : Std(post-pre) = 6.4

whilst the Reachman: Std(post-pre)= 13.7 . These results are shown graphically in figure 6.5

Table 6.4: Summary of Results of the FMA score pre and post intervention.

Group	Sample Size	Pre Treatment				Post Treatment				Within Person Difference (Diff= Post – pre)			
		Median	IQR	Mean	SD	Median	IQR	Mean	SD	Median	IQR	Mean	SD
Robot	19	18	13	17	10	37	31	36	17	15	24	18	14
Control	18	20	14	20	14	33	33	28	17	6	9	8	6

Figure 6.4 Bar graph demonstrating total FMA scores pre and post intervention for both groups

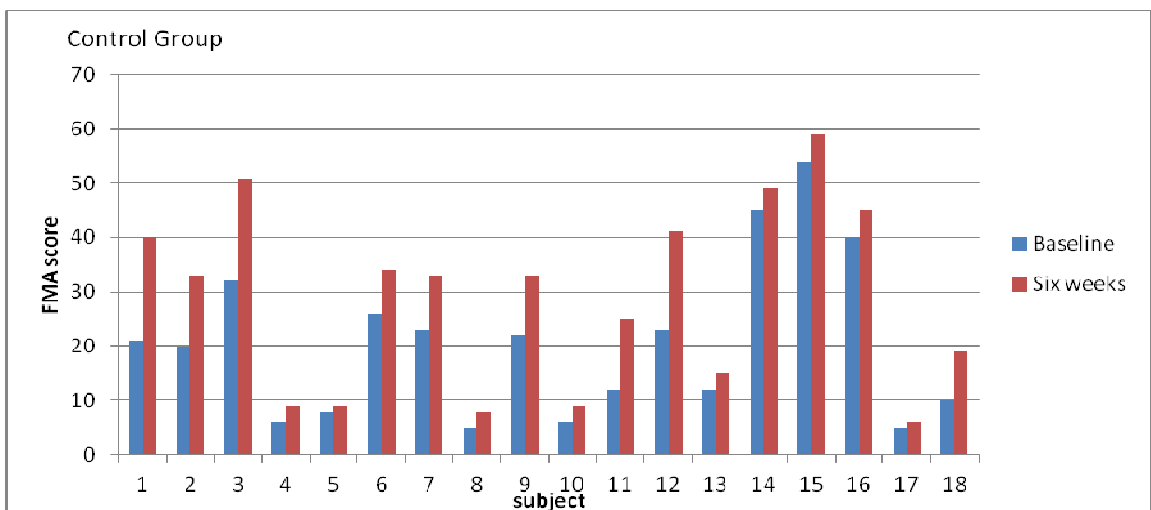
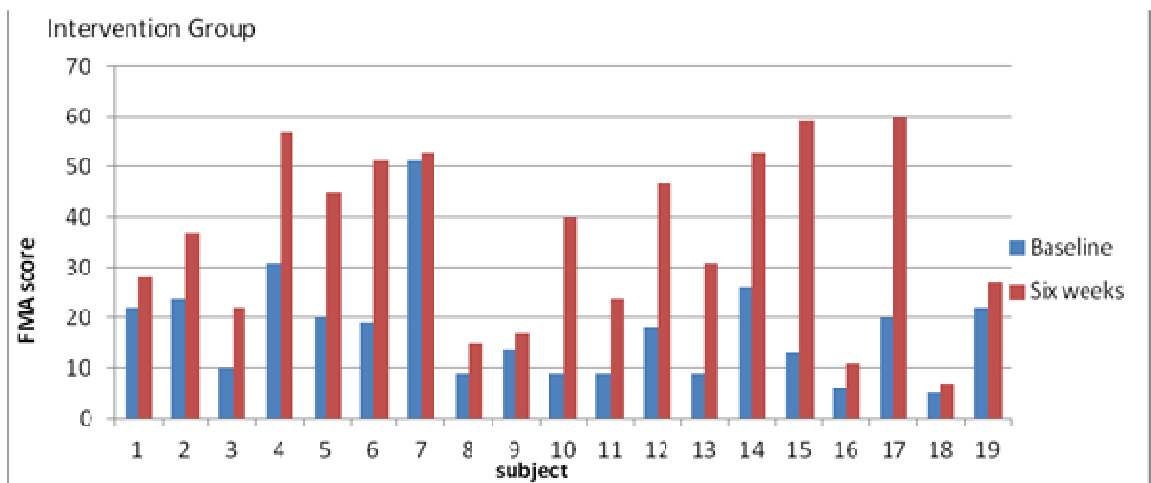
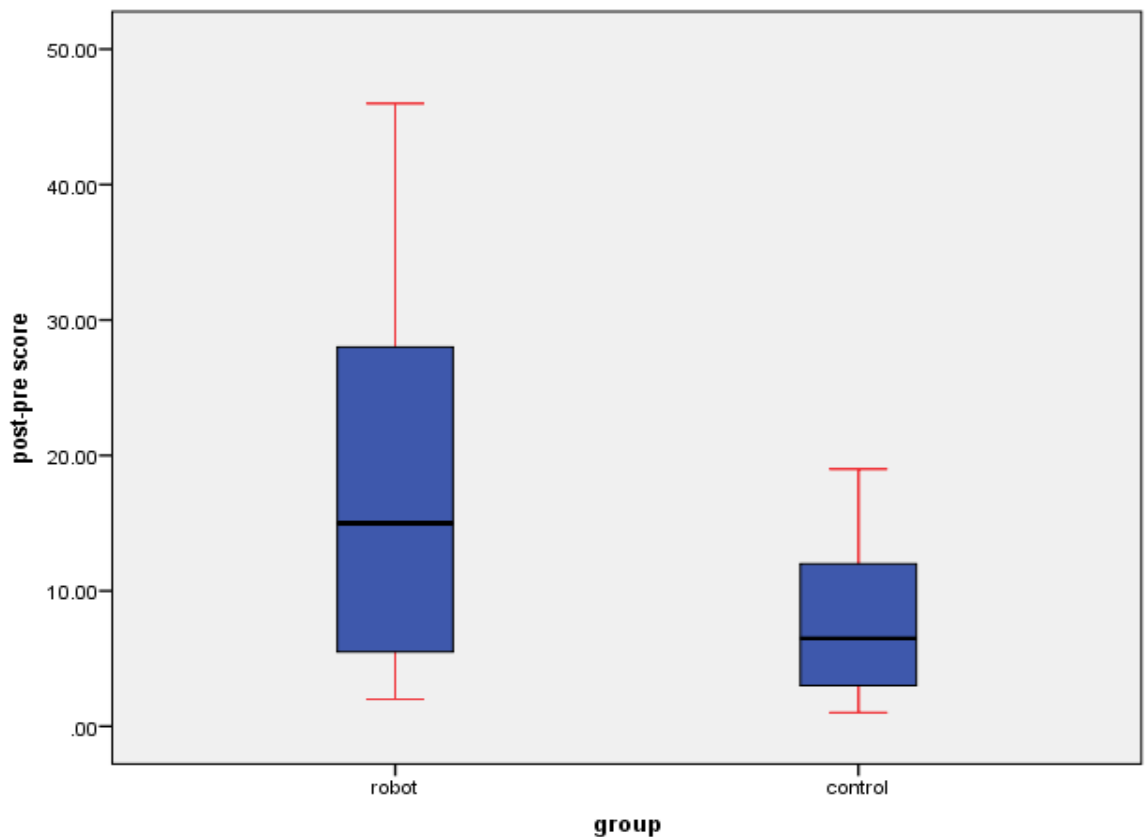
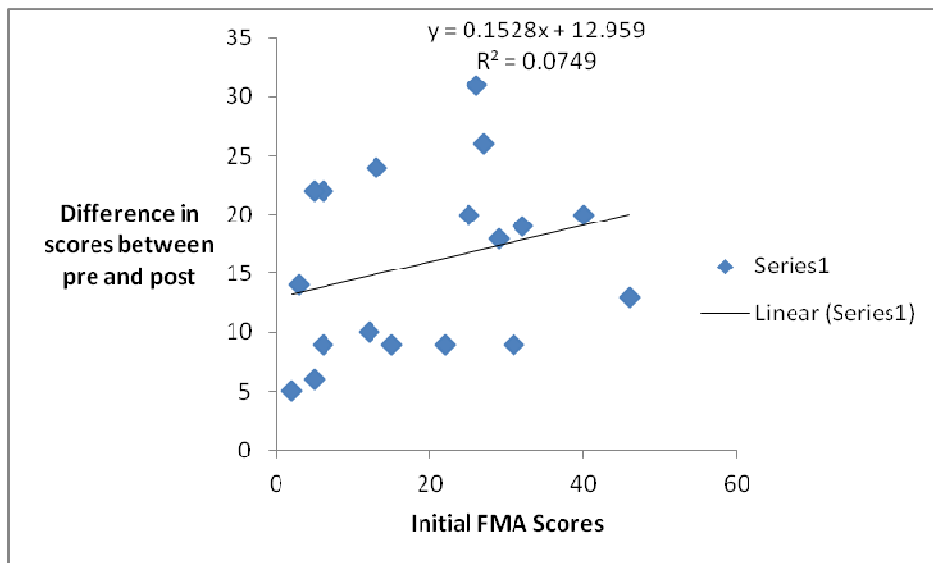


Figure 6.5- Box plot showing differences in FMA scores in both groups

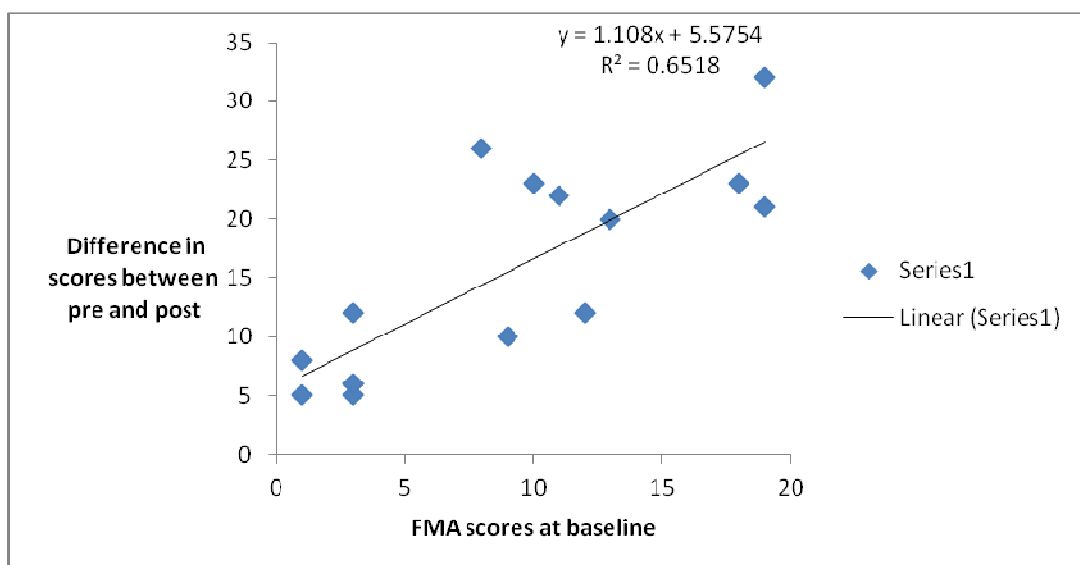


A sub analysis of FMA scores was carried out to look for any relationships in the data. In particular a sub-group analysis was completed to assess whether people levels of function impacted on how much improvement they made following the intervention and whether this was different in the two groups. Although it was recognised that power would be lost by analysing this sub-group separately, it was considered that it might provide important information on trends in the data. Correlations were performed using the non-parametric Spearman's Test. A correlation was carried out comparing subjects baseline FMA scores and the difference in scores between pre and post FMA scores following the intervention period. This can be seen in graph 6.1. In the graph below the subjects with high FMA scores were removed from the correlation

Graph 6.1: Correlation between FMA scores at baseline and difference in scores following intervention in the robotic group



Graph 6.2: Correlation between FMA scores at baseline and difference in scores following intervention in the control group



A statistically significant relationship was found on correlation in the control group, whilst this was not seen in the ReachMan group. This suggests that subjects in the control group with better movement initially made better gains in movement following a treatment

intervention (this would be expected). However this does not seem to be the case in the Robot group, where there does not seem to be a correlation between better movement (higher FMA scores) and improved scores following use of the device. This suggests that the robot can cause improvement in arm movement in patients with very little movement as well as patients with more movement initially and may explain the increase in SD in the intervention group.

Three subjects in study presented with mild upper limb weakness (FMA scores on baseline above 40). Chapter 5 found that subjects with milder arm impairments found using the device less beneficial (it did not seem to challenge them enough). Therefore a further subgroup analysis with these subjects removed from analysis was also performed. This found the same results as a the full group analysis i.e no statistically significant change was seen between the control and the intervention group ($p=0.67$)

SECONDARY OUTCOME MEASURES

ARAT

The secondary outcome measure was the ARAT, which is also an ordinal scale. The data from this outcome were not normally distributed. The non-parametric statistical tests that were used to evaluate the results of the FMA have therefore been used to analyse these results.

Table 6.5 Baseline and outcome ARAT scores by group

ARAT scores by allocated group		
Group	Median Baseline ARAT (IQR)	Median Outcome ARAT (IQR)
Control: no treatment (n 18)	1(6)	3(13)
ReachMAN (n 19)	1(4)	6 (15)

No significant difference was seen between the control and Reachman groups at the start of study Wilcoxon rank-sum test ($p=0.620$). Significant changes in pre and post scores of

both control and Reachman Wilcoxon signed-rank test was seen ($p=0.000$), but just as in the FMA scores there was no statically significant difference between the control group and the intervention group ($p=0.518$). Figure 6.6 shows subjects initial and final ARAT scores and illustrates that both groups improved in the measure from initial assessment following the six week interval. As in the FMA outcomes, generally higher improvements were seen for subjects who used Reachman in comparison to the control group (Control : $\text{std}(\text{post-pre}) = 7.282$ Reachman: $\text{std}(\text{post-pre})= 12.13$) this can be seen visually in the box plot below (figure 6.8). Although higher improvements can be seen these are not nearly as large as the difference seen between the groups in the FMA score.

Figure 6.6: Bar graph demonstrating total ARAT scores pre and post intervention for both groups

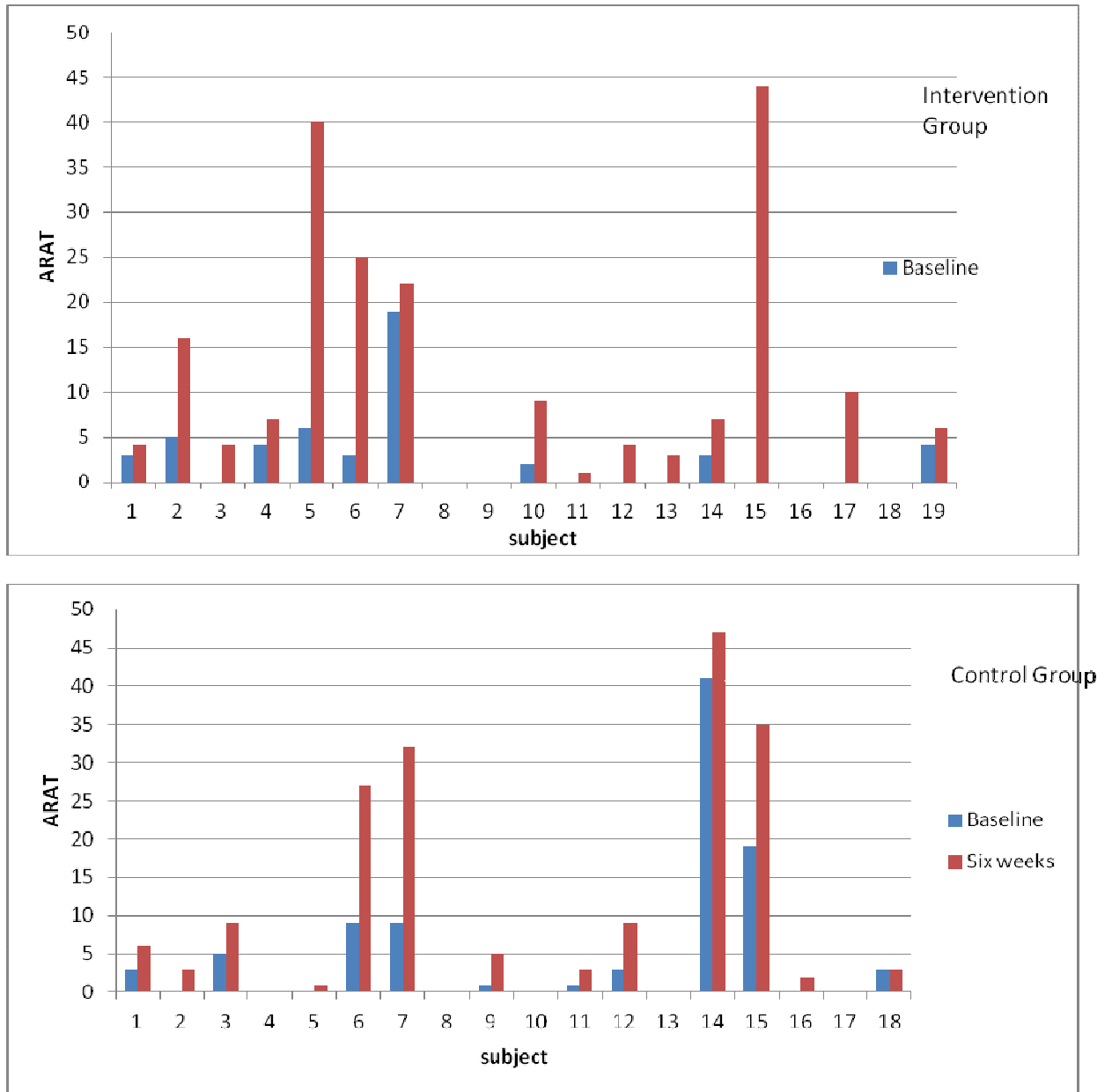
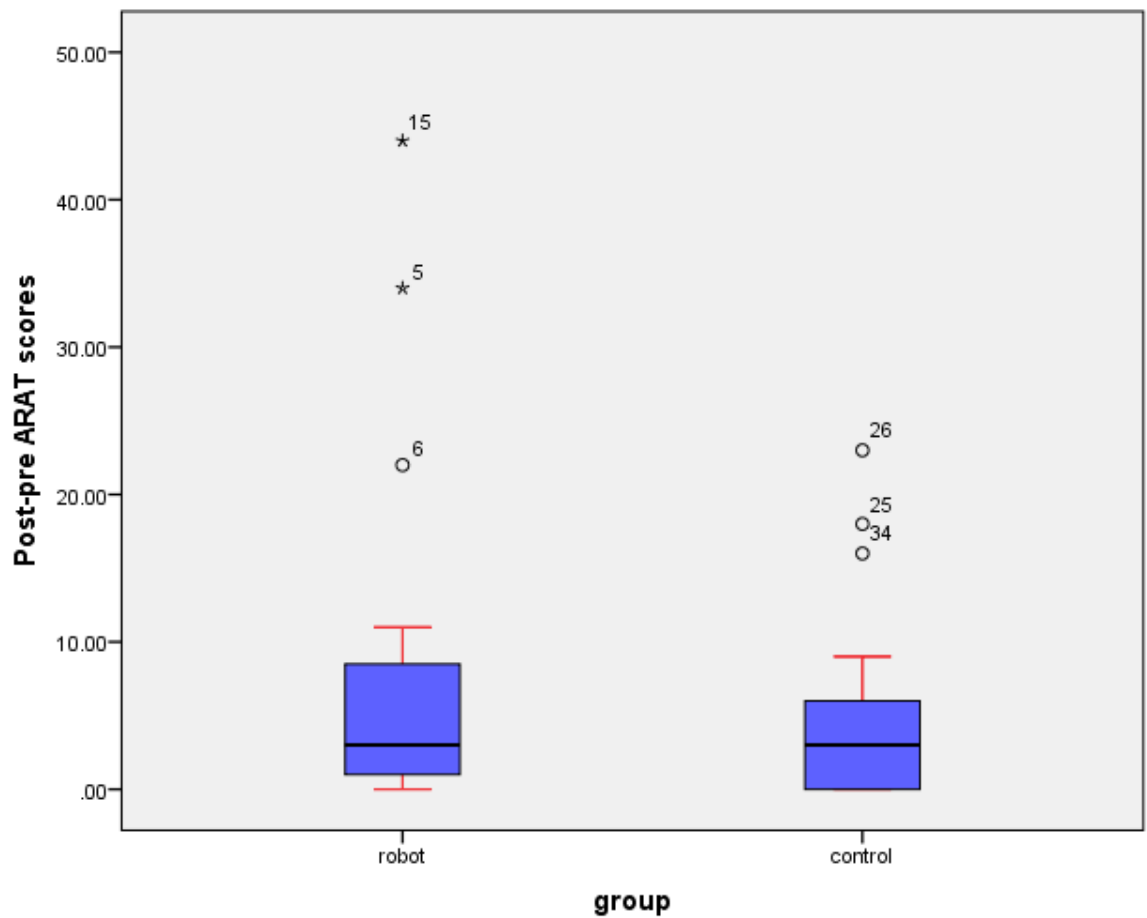


Figure 6.7 Box plot showing differences in ARAT scores in both groups



CHEDOKE HAND AND ARM INVENTORY (CHAI)

The data from this outcome were also not normally distributed. The non-parametric statistical tests that were used to evaluate the results of the FMA were used to analyse these results.

Table 6.6 Baseline and outcome CHAI scores by group

CHAI scores by allocated group		
Group	Median Baseline CHAI (IQR)	Median Outcome CHAI(IQR)
Control: no treatment (n 18)	13(13)	17(26)
ReachMAN (n 19)	13(13)	26(39)

Wilcoxon rank-sum test analysis found no significant difference between control and Reachman population at the start of study ($p=1.00$). Significant change in pre and post scores of both control and Reachman were however found using the Wilcoxon signed-rank test ($p=0.0001$)(as was expected this illustrates that all subjects improved in their arm movements and functional abilities following the six week trial period). Just as in the previous scores there was however, no statically significant difference between the control group and the intervention group ($p=0.343$) . Generally higher improvements were seen for subjects who used the Reachman device in comparison to the control group. (Control : $\text{std}(\text{post-pre}) = 8.22$, Reachman: $\text{std}(\text{post-pre})= 16.88$). Standard deviation of difference between pre and post results of ReachMAN is higher than the pre-post difference in control group and notably this was much higher than seen in the ARAT. This is shown graphically in figure: 6.9

Figure 6.8: Bar graph demonstrating total CHAI scores pre and post interventions in both groups

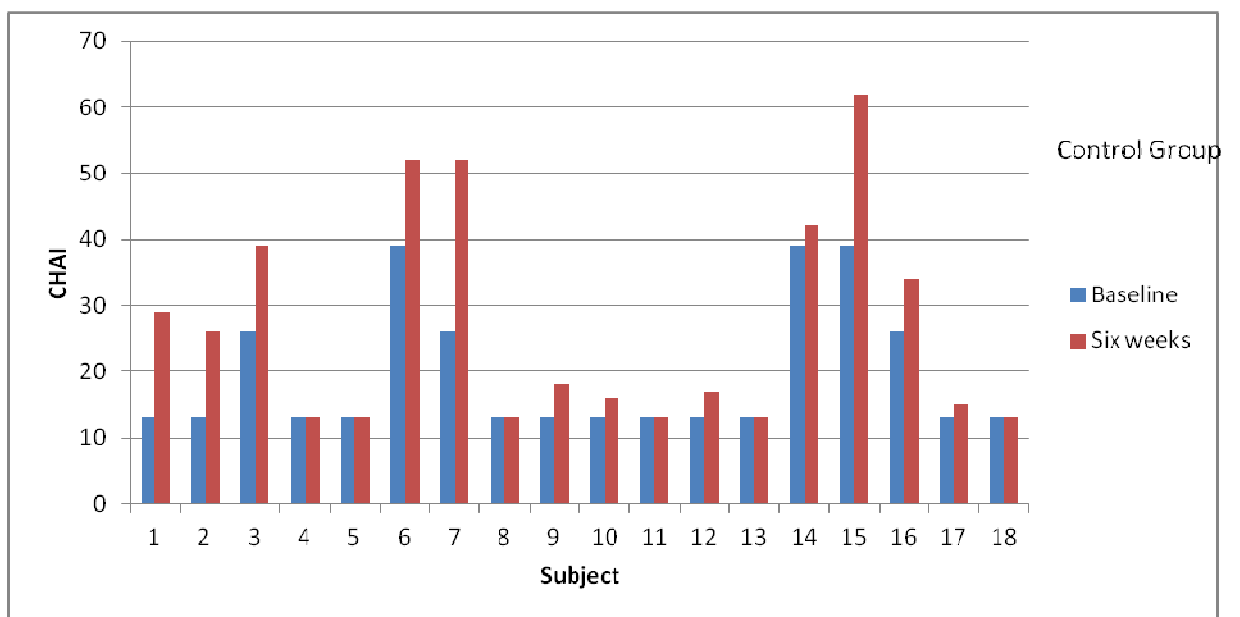
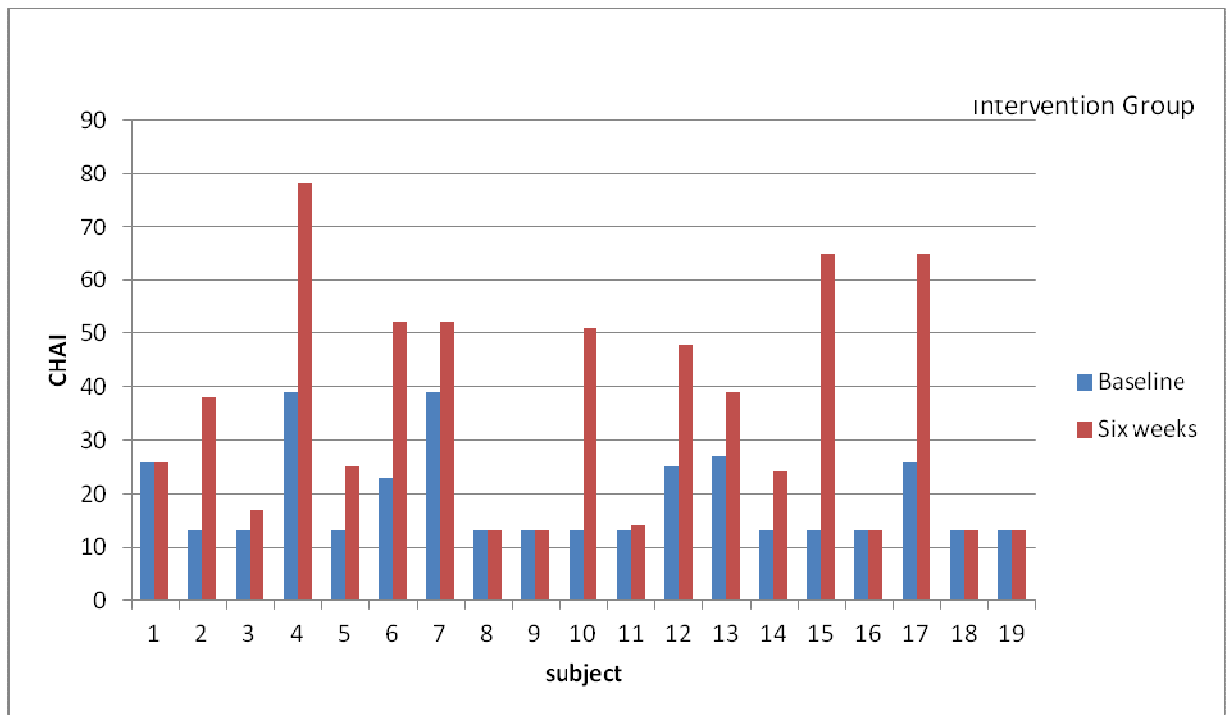
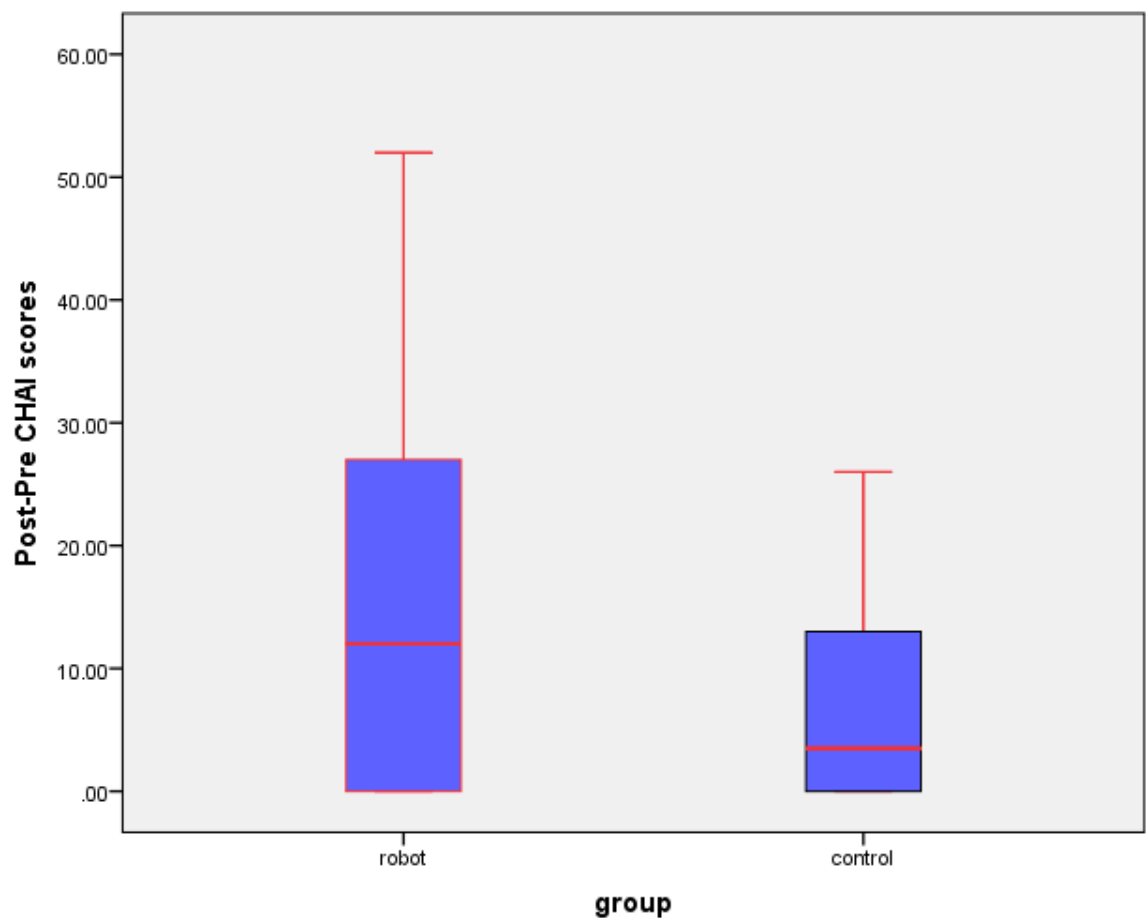


Figure 6.9 Box plot showing differences in CHAI scores in both groups



STREAM

The control group had slightly lower median scores on baseline than the control group (indicating more impairment in their arms).

Table 6.7: Baseline and outcome STREAM scores by group

STREAM scores by allocated group		
Group	Median Baseline STREAM(IQR)	Median Outcome STREAM (IQR)
Control: no treatment (n 18)	5(8)	7(11)
ReachMAN (n 19)	7(6)	10 (6.5)

However Wilcoxon rank-sum test analysis found no significant difference between control and Reachman population at the start of study ($p=0.927$). Significant change in pre and post scores of both control and Reachman were however found using the Wilcoxon signed-rank test ($p=0.000$)(as was expected this illustrates that all subjects improved in their arm movements and functional abilities following the six week trial period). Just as in the previous scores there was however, no statically significant difference between the control group and the intervention group ($p=0.385$). Generally higher improvements were seen for subjects who used the Reachman device in comparison to the control group. Standard deviations of the difference between pre and post results of ReachMAN is higher than the pre-post difference in control group (Control : $\text{std}(\text{post-pre}) = 1.4$, Reachman: $\text{std}(\text{post-pre})= 2.5$). This is shown graphically in figure: 6.11

Figure 6.10: Bargraph demonstrating total STREAM scores pre and post intervention in both groups

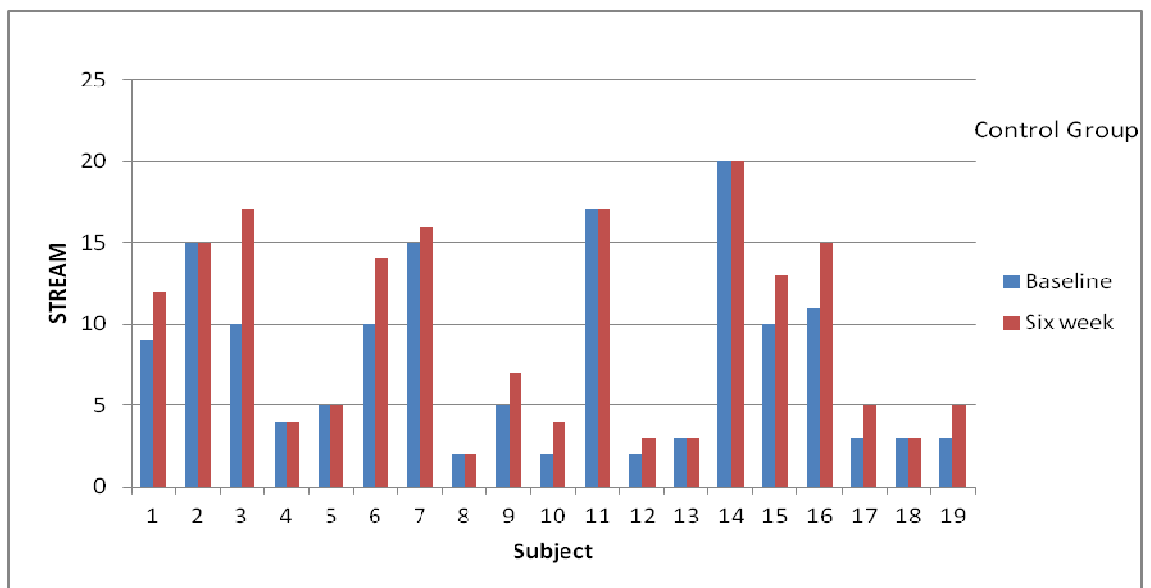
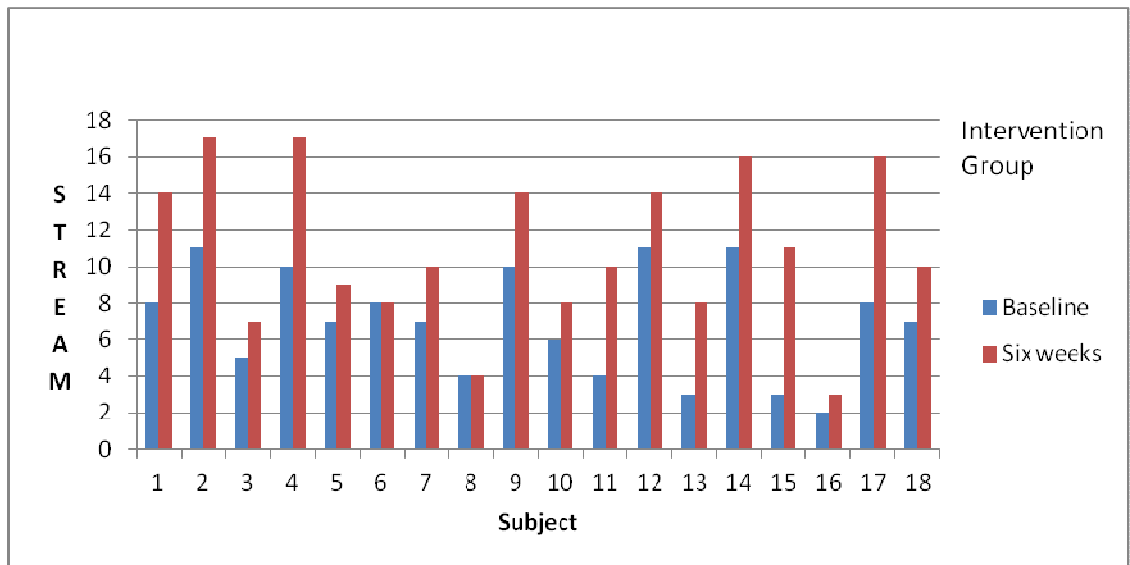
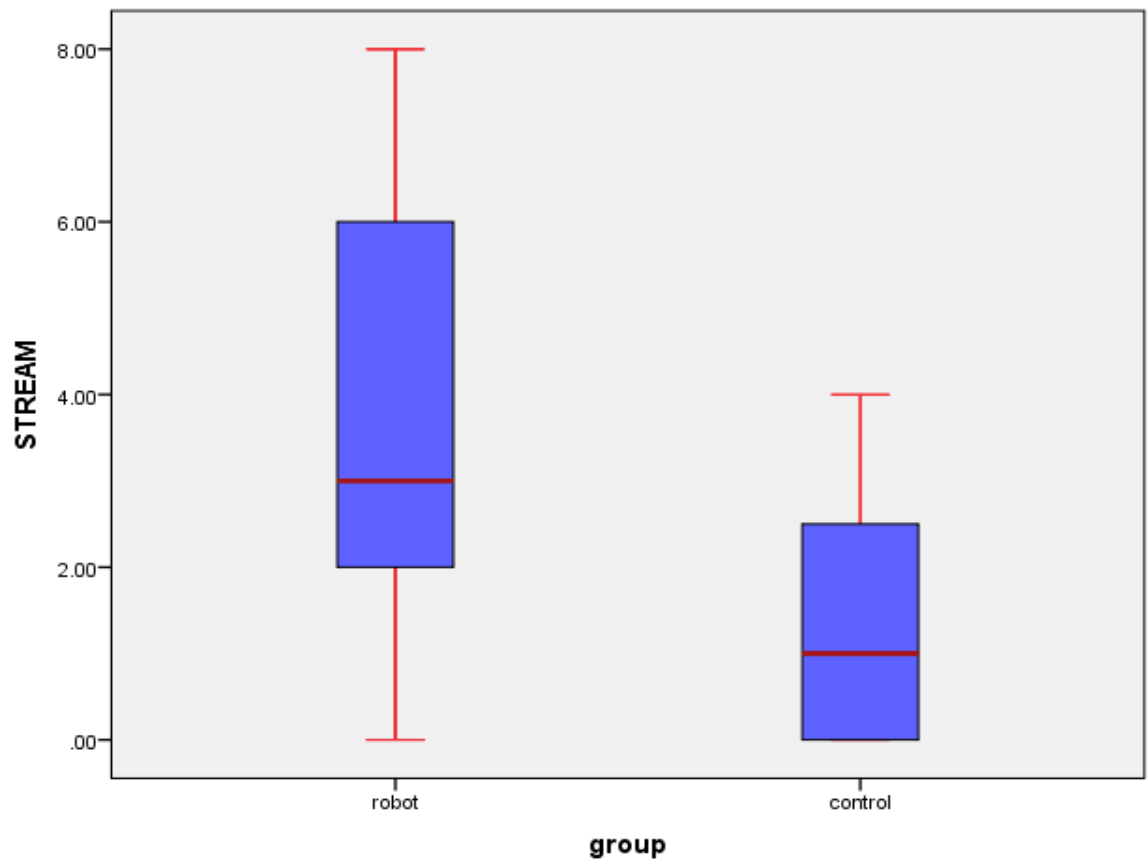


Figure 6.11 Box plot showing differences in STREAM scores in both groups



PATIENT REPORTED OUTCOME MEASURE

DASH

The control group rated themselves as higher levels of arm impairments initially in comparison to the robot group, although IQR (18) for both groups) were the same.

Table 6.8: Baseline and outcome DASH scores by group

DASH scores by allocated group		
Group	Median Baseline DASH (IQR)	Median Outcome DASH (IQR)
Control: no treatment (n 18)	63(18)	56(17.9)
ReachMAN (n 19)	57(18)	45 (19)

No significant difference was seen between the control and Reachman groups at the start of study Wilcoxon rank-sum test ($p=0.822$). Significant changes in pre and post scores of both control and Reachman on Wilcoxon signed-rank test was seen ($p=0.0001$), but just as in the FMA scores there was no statically significant difference between the control group and the intervention group ($p=0.142$) Figure 6.12 shows subjects initial and final DASH scores and illustrates that both groups improved in the measure from initial assessment following the six week interval (The DASH scores are in reverse to the previous measures mentioned. Therefore a decrease in scores illustrates better perceived improvements in arm function). As in the FMA outcomes, generally greater improvements were seen for subjects who used Reachman in comparison to the control group (Control : $\text{std}(\text{post-pre}) = 7.76$ Reachman: $\text{std}(\text{post-pre}) = 10.6$) this can be seen visually in the box plot below (figure 6.13).

Figure 6.12: Bargraph demonstrating total DASH scores for pre and post intervention in both groups

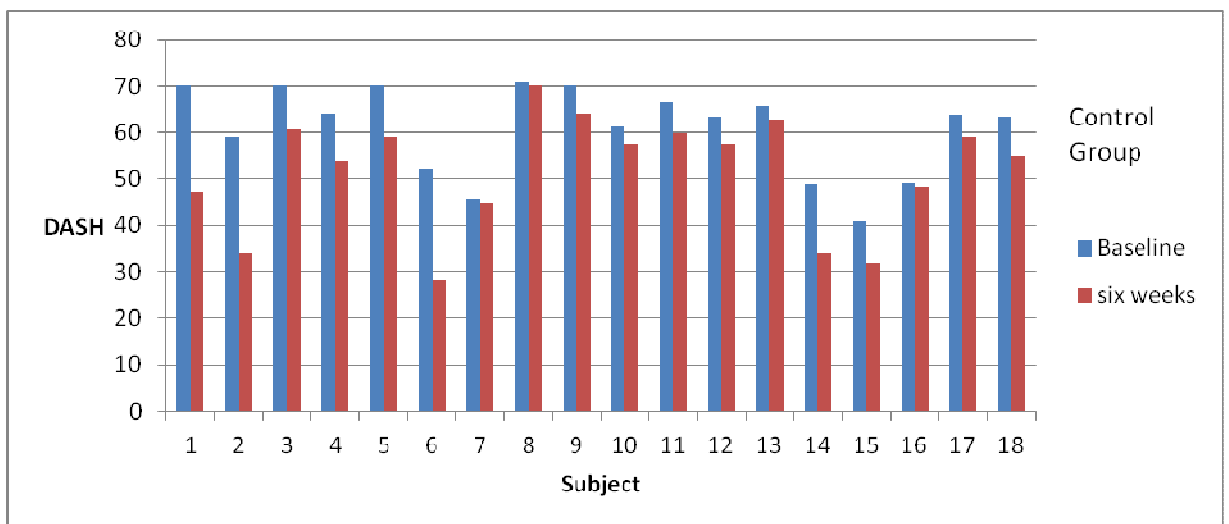
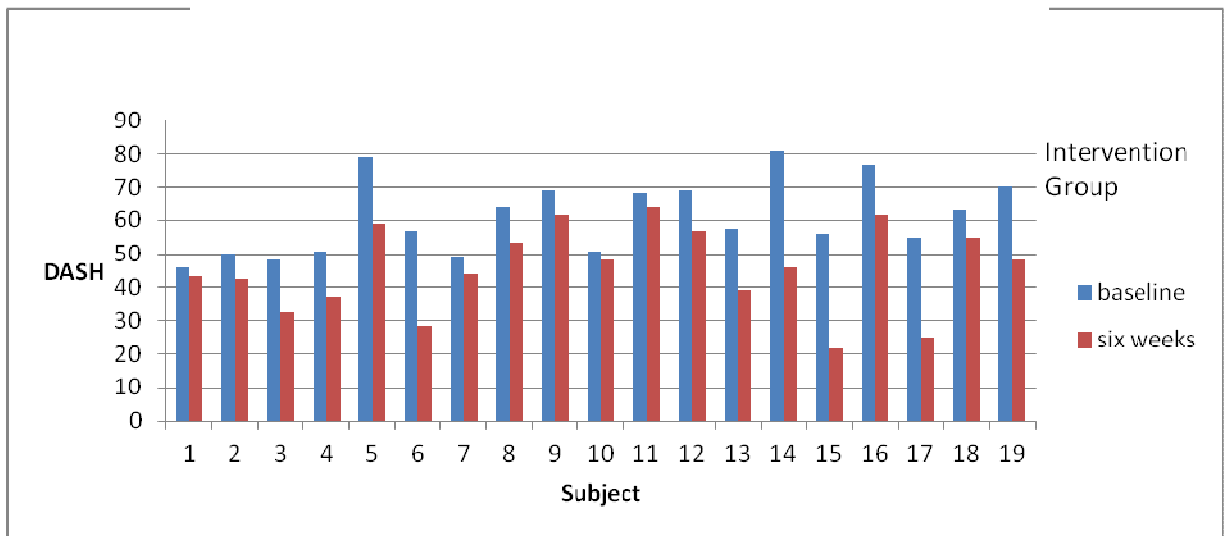
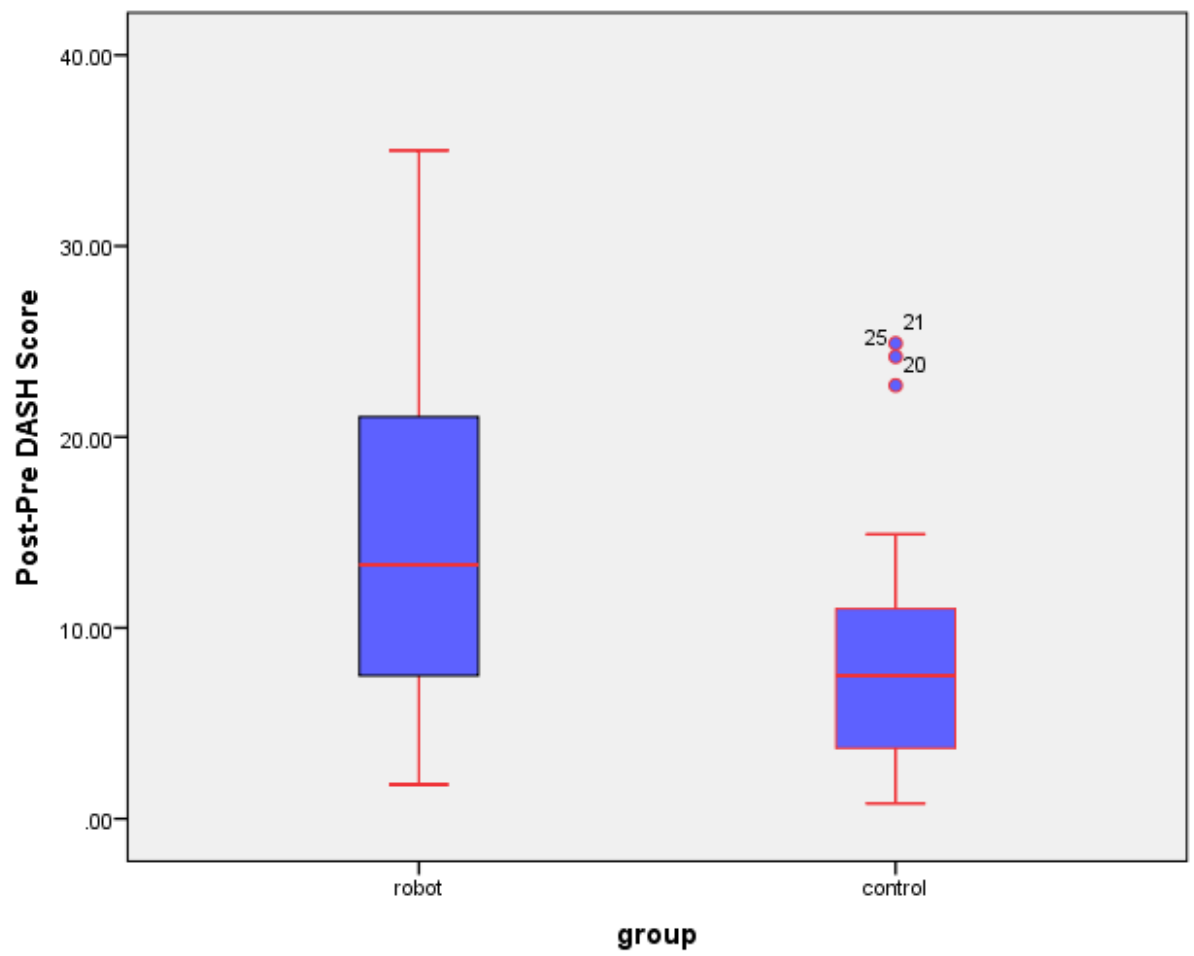


Figure 6.13 Box plot showing differences in DASH scores in both groups



ABILHAND

Each individual ABILHAND question score was processed through the web site: <http://www.rehab-scales.org/abilhand-rasch-analysis-chronic-stroke.html> this provides online analysis which converts the raw scores of the ABILHAND questionnaire into a linear measure of manual ability. Statistical analysis using SPSS version 21 was then carried out of the logit scores pre and post intervention for each subject. This found no significant difference between the control and Reachman groups at the start of study using Wilcoxon rank-sum test ($p=0.78$). Significant changes in pre and post scores of both control and ReachMAN Wilcoxon signed-rank test were seen ($p=0.000$)

Unlike the other measures a **statically significant** difference was also seen between the control group and the intervention group ($p=0.042$).

Table 6.9: Summary of Results of ABILHAND scores pre and post intervention.

Group	Sample Size	Pre Treatment				Post Treatment				Within Person Difference (Diff=Post–Pre)			
		Median	IQ R	Mean	SD	Median	IQ R	Mean	SD	Median	IQ R	Mean	SD
Robot	19	-0.15	.82	-1.2	2.2	0.27	.85	0.36	17	0.9	1.5	1.5	1.9
Control	18	-0.17	5.9	-1.9	2.8	-0.09	1.3	-0.44	17	0.5	2.1	1.5	1.9

Table 6.10 Baseline and outcome Barthel Index scores by group

Barthel Index scores by allocated group		
Group	Median Baseline Barthel(IQR)	Median Outcome Barthel (IQR)
Control: no treatment (n 18)	11 (12)	5 (5)
ReachMAN (n 19)	14 (12.5)	6 (10)

The data from this outcome were also not normally distributed. The non-parametric statistical tests that were used to evaluate the results of the FMA were used to analyse these results. In similarity to the other measures used in the study, no significant difference was seen between control and Reachman population at the start of study using Ranksum test ($p=0.425$). Significant change in pre and post scores of both control and Reachman were seen with the Wilcoxon signrank test ($p=0.001$) However no significant changes were seen between the groups ($p=0.940$). Generally higher improvements for subjects who used Reachman compared to the control group : $\text{std}(\text{post-pre}) = 2.79$ Reachman: $\text{std}(\text{post-pre}) = 4.05$ but as the measure was looking at the general functional abilities of the subjects it was not expected that there would be a significant change between groups with the intervention.

Table 6.11 Baseline and outcome EQ5D scores by group

EQ5D scores by allocated group		
Group	Median Baseline EQ5D (IQR)	Median Outcome EQ5D (IQR)
Control: no treatment (n 18)	0.55 (13)	0.61(16)
ReachMAN (n 19)	0.55(14)	0.61(13)

The data from this outcome were also not normally distributed. The non-parametric statistical tests that were used to evaluate the other measures were used to analyse these results. In similarity to the other measures used in the study, no significant difference was seen between control and Reachman population at the start of study using Ranksum test ($p=0.675$). Significant change in pre and post scores of both control and Reachman were seen with the Wilcoxon signrank test ($p=0.000$). However no significant changes were seen between the groups ($p=0.964$). 100% of the REACHMAN subjects improved in the score following the period of intervention, while 89% of control subjects reported improvements. Just as in the Barthel Index the measure was looking at the general functional abilities of the subjects, it was not expected that there would be a significant change between groups with the intervention.

OTHER MEASURES

ASHWORTH

Mean and Median Ashworth scores for the subjects at baseline was 2. No participants Ashworth changed during the intervention period.

6.8.8 POWER CALCULATION

One of the aims of this exploratory study was to be able to use the data to perform a power calculation to explore sample size for a definitive RCT. This calculation was performed on the basis that each group would need to show a clinically important difference of 5 points in FMA score (This is based on the largest RCT performed (Lo et al (2010) ¹⁷¹) looking at a robotic device compared to normal therapy, which used this marker for clinically importance difference) between the mean within person differences. The power calculation for 5% significance and 80% power predicted a definite study would need 73 subjects in each group. This power calculation was performed by Pauline Rodgers statistician at UCL].

6.9 DISCUSSION

The main implications of the trial will be now be considered and an analysis of the results will be presented here in relation to the research questions

6.9.1 RESEARCH QUESTIONS

What are the effects of using a robot on the motor performance of the hemiplegic upper limb in the sub-acute phase after stroke?

The results of the study did not lead to a complete rejection of the null hypothesis. All groups, including the control, improved from baseline to outcome. The changes seen in the groups may have been due to natural recovery. Only one measure-the ABILHAND demonstrated statistically significant improvement when comparing the intervention to the control. This was not seen with the primary outcome measure the FMA. However there is a suggestion of positive trend in the invention group as a there was a larger difference seen between pre and post results in the ReachMAN group than in the control group with the FMA and the other outcome measures.

This finding has similarities to the findings in previous literature evaluating the use of robotic device in the acute/sub acute phase (as discussed in Chapter Two). Nonetheless those studies found a statistically significant improvement in FMA scores with use of a robotic device ^{171;186;200;317} while this was not seen in this exploratory RCT (only a trend of

higher improvements was seen in this measure.) In contrast to those studies^{171;186;200;317} this study does also suggest a trend (with a statistical significance in a PROM) for functional and patient perceived improvement in arm function with use of the device. However the other studies did not use specific activity or participation measures in their studies so we are unable to make this direct comparison.

Interestingly the ABILHAND was the only measure that demonstrated a statistical significance difference between the control and robot groups. This measure was one of the three measures from the systematic scale selection that was chosen and best met the psychometric criteria used (as described in Chapter Four). This could indicate that this scale was sensitive to change seen with the intervention. However due to the small sample number and that this was the only measure that did find statically significant change, this result must be treated with caution.

It is likely that *clinically* significant changes are of greater importance to people with stroke and the therapists who treat them than purely *statistically* significant ones. A change that is statistically significant but which has little or no impact on the functional ability of the person's arm is likely to be less important than a non-statistically significant change that involves an improvement in the use of the limb. The clinical significance of changes in the values obtained with the outcome measures used in this trial is difficult to assess. In a population starting at a very low level, small changes may be neither statistically significant nor result in a change in functional use of the upper limb. These changes may however indicate a response to the intervention and may therefore be of clinical significance; in particular, they may make it possible for an individual to participate in, or to benefit from, other therapeutic interventions that require more active participation.

Little work has been completed on the clinical significance of changes as measured by the battery of scales used. In a study of the reliability of the ARAT, van der Lee et al (2006)²⁸⁴ suggest that the "minimal clinically important difference" (MCID) on the scale was a change of 5.7 points (10% of total score). This was reported to be based on clinical experience and estimates from literature relating to outcomes in respect of spinal manipulation. More recently, Lang et al (2008)³¹⁸ estimated the MCID of a number of upper limb outcomes in the context of a trial of CIMT in the sub-acute stroke population.

They conclude that MCID values for the limb vary between 12 and 17 points on the ARAT, depending on whether the stroke affects the dominant or the non-dominant hand. Recent literature has also looked at the MCID in FMA UL scores. Arya et al (2011)³¹⁹ looked at 71 subjects poststroke (mean duration, 8.42 weeks after stroke). They found that patients who achieve a 9 to 10 point increase in FMA score are more likely to experience or perceive a meaningful and clinically important improvement in their disability level than those who do not. However Page et al (2012)³²⁰ looked at one hundred forty-six individuals with chronic, mild to moderate upper-extremity (UE) hemiparesis and found that the estimated MCID of the score ranged from 4.25 to 7.25 points. Further discussion on this and on the scales use in this study will be given in Chapter Nine

Participants only used the device for short periods (20 minutes) of time. This is less than in other clinical trials of robotics which have used intervention protocols of 30-60 minutes per day^{205,206,171}. However, these trials were carried out in a chronic stroke population, with patients more than six months after stroke and already discharged from inpatient rehabilitation. The participants in this study commenced using the robotic device within six weeks of their stroke and were concurrently engaged in an intensive, multidisciplinary inpatient neurorehabilitation programme. The intensity of the rehabilitation combined with the early stage post stroke may explain why participants were only able to tolerate short periods on the robot. Doornebosch et al (2007)²²⁶ et al reported similar findings, in sub-acute patients who used a robotic device for on average 20 minutes a day, (when fatigue prevented using the device for longer periods). Frequent, short sessions may have suited the subjects better and may have been a way of delivering more intervention.

Preliminary data from the robotic device suggest that participants performed 200-300 trials of arm movements during the robotic sessions. Literature is inconclusive as to the exact number of upper limb movements post stroke that promote functional recovery although 300 and 800 repetitions per session has been suggested³²¹. The participants in the intervention group in this study performed less than this recommended amount, however it is not known how many arm repetitions the subjects in the control group performed. It may have been that it is due to the small number of repetitions that no significant difference was found between the groups. However, as the results do suggest trends toward the intervention leading to better upper limb recovery, it may be that even a small increase in arm repetitions can improve arm function.

What severity of arm impairments could use the device and is there a difference in the potential benefit of the aid depending on the severity of arm paresis?

The current literature looking at the effect of robotic devices on upper limb recovery, does not suggest that a particular level of activity in the arm leads to better improvements with use of robotics. However a middle range of motor impairments (falling between fifteen and 23 inclusive on the proximal FMA) has been implicated to be the optimal for robotic intervention ¹⁷⁴. The results of this trial however on sub hoc analysis of the difference in FMA score within subjects from pre to post this found there did not seem to be a correlation between better movement (higher FMA scores) and improved scores following use of the device. This suggested that the robot can cause improvement in arm movement in patients with very little movement as well as patients with more movement initially. However, as this is a *post hoc* analysis of the small sample size used in the study the results must be viewed with caution.

Subjects in the robotic group with higher FMA scores seemed to make fewer improvements during the intervention. This fits with the data seen in the first phase of the study, where subjects with minimal upper limb impairments were able to interface with the robotic device but found it did not challenge them sufficiently. This could also however be indicative with problems with the outcome measurement scales, with ceiling effects with the FMA.

On a practical level patients with very little arm movement could use the machine. (Their perceptions of the use of the device are explored in the subsequent chapter.) This has clinical implications and could be of clinical importance as currently there is little in way of therapy for people with severe arm paresis and the use of a robotic device such as the ReachMan device, may be a way of delivering increased intensity of therapy, and repetition of movement (as recommended for upper limb recovery) in these severely impaired individuals.

What resources are required in terms of staffing for use of the machine?

Rehabilitation Assistants were able to provide supervision to the subjects when using the device and it was found to be both a practical and feasible intervention as an addition to the therapy the participants were receiving on the rehabilitation units. Time was needed from a trained physiotherapist to instruct the rehabilitation assistants how to adapt the program, adequately position the subject and which level to use on the device. Whilst regularly monitoring of how the invention was going was also needed. Unfortunately the device was unable to be used by patients independently and therefore a member of staff was needed at all treatment occasions. The device broke down on several occasions during the study period and this resulted in lost sessions on the device. The cost of the device in terms of therapist training, therapy and RA and the time involved in the provision of the therapy should be considered in future evaluation of the intervention. Furthermore taking into consideration the cost of maintenance of the device and call out for repairs is also required.

Power Calculation

An aim of this exploratory study was to provide a sample size for a definite RCT. Although no statistical effect was found, with the intervention, a power calculation for 5% significance and 80% power predicted using the results from the FMA score, a definite study would need 73 subjects in each group. This is relatively low numbers for a definitive RCT and again is suggestive that the results seen implicit benefit from the experimental intervention.

6.9.2 METHODOLOGICAL LESSONS LEARNED FROM THE PRESENT TRIAL

It is necessary to note aspects of the design of the study that worked well and should be included in future studies and aspects that require modification.

The study design used in the trial has its limitations. Both control and subjects received conventional therapy, however only the robotic group participated in additional upper limb therapy (use of the device). Therefore it is difficult to differentiate if the trends for improvement seen in the study with the robot were due to the intervention per se or whether this was due to subjects receiving additional therapy.

Ideally a third intervention group should have been added to the study. This group would have dose-matched practice of arm movements, to address the unanswered question as to whether subjects improved due to increased intensity or an specific effect of using the robotic itself.

. However 20 min of daily additional therapy use is a very short amount of time as previously discussed and this again could hint to the improvements seen being specific to the experimental intervention.

The number of treatment sessions that were missed or reduced in length due to other ward commitments (e.g. treatments, meals, investigations, visitors) challenges the view that stroke patients spend long periods unoccupied. The team also noted high level of fatigue in the participants. It is thought that sleep may play an important role in motor recovery after stroke ³²², and so providing sufficient periods of rest may be vital. Future studies of the intervention may therefore need to consider the length and frequency of treatments.

Conventional Therapy

It had been hoped to include an analysis of the amount of conventional therapy received by the participants. Unfortunately, too few treatment records were completed to make this possible. It was not therefore possible to assess the impact of conventional therapy on the outcomes. As the therapists were not blind to group allocation, it is possible that the participants in the control group received additional conventional therapy for the upper limb, thus introducing a source of bias. Ways of capturing more information on the conventional therapies for the upper limb provided during the trial should be developed for future research studies.

6.9.3 SOURCES OF ERROR

The results may be subject to Type II error, where a treatment effect is present but is not identified by the trial, due to inadequate power or inappropriate analysis. Type II error (false negative) relates to sensitivity. The use of ordinal scales and non-parametric statistical tests may increase the chance of Type II errors.

Wade (2001)³²³ discusses the difficulty of evaluating rehabilitation interventions, and suggests that failure to demonstrate a change due to one element of the rehabilitation package may be because it is interdependent with the other elements and may only have a small independent effect. He defines this as a 'Type III error'. It is possible that this trial could be at risk of Type III error. All participants received the normal stroke unit care and any additional benefit of using ReachMan may have been too small to measure using the outcome measures chosen.

LIMITATIONS OF THE STUDY

POPULATION SIZE

The study was an exploratory RCT, with a small population size therefore results were interpreted cautiously and considered as hypothesis generating rather than providing conclusive results.

RECRUITMENT

Recruitment to research studies in the acute setting is always likely to be challenging, as the potential participants are often acutely unwell and are adjusting to their new circumstances after stroke. Due to the ethical approval for the study being for a single site a large number of patients were from out of area and therefore unable to be recruited. The trend for shorter hospital stays after stroke, with discharge to either intermediate care facilities, or home with the community therapy meant that some people were discharged and the study was unable to provide the facilities to allow them to come in for daily use of the robot. UCLH hospitals have a large number of research trials ongoing simultaneously and therefore recruitment was also affected by the co-recruitment of other upper limb research studies. The low proportion of eligible patients participating limits the generalisability of the trial. The recruitment figures for this study were however higher than other studies that have looked at upper limb rehabilitation.. In a recently completed trial of the Armeo robot, for example ³²⁴ of 393 stroke patients who were screened over an 8-month period 3.1% were recruited. Whilst Donaldson et al ¹⁴⁰, report a recruitment rate of 8.1% and a refusal rate of 14.3% to a study of Functional Strength Training for the upper limb after stroke.,

The baseline data of the subjects recruited to the study showed that population distribution did not match normal distribution, with there being higher than normal stroke survivors in 20-30 age range. This may have been site specific as one of the rehabilitation units the subjects were recruited from is a level 3 unit and tends to take younger patients who need a longer period of rehab than that usually afforded in stroke rehab services. However, the ages were equally distributed between the groups, but this does also limit the generalisability of the findings.

ATTRITION

The trial had a good completion rate, although one participant did withdraw voluntarily, although outcome measures were completed in all this case.

BLINDING

No blinding was used in this study. The nature of the intervention (the use of a robotic device) meant that it was not possible to blind either the participants or the therapists to the allocation group. However outcome assessors could have been blinded to group allocation. Future studies should include assessor blinding.

The lack of blinding in the study is a significant limitation and should definitely be addressed in any future studies.

STRATIFICATION

Sub-hoc analysis of the FMA scores suggested a difference with the intervention depending on the severity of arm impairment. It would therefore be useful to explore this further in future studies by stratify subjects into impairment levels. The analysis also suggested that participants with higher level of FMA scores (nearer to the maximum score) benefited the least from the use of the robot, so a consideration could be to exclude these subjects from future studies.

OUTCOME MEASUREMENT

The outcome measures were mostly taken on the day after the final intervention. Francis et al (2004) ³²⁵ suggest that functional outcomes after an intervention to treat spasticity in

stroke may not reach the maximum value immediately after treatment, and propose that a follow-up measure should be completed. The rationale for completing a single outcome was that any change from the start of the intervention would be identified by a measurement after the final robotic intervention and there is no current literature that suggests that the effect of robotics is not immediately seen. Future studies may benefit from a follow-up measure to evaluate whether participants consolidate any improvements due to the intervention with subsequent independent use of the limb.

Following the study limitations were found with the outcome scales selected in the participant population used. Further analysis of the outcome measures in the context of this study investigation is included in Chapter Eight.

6.10 CONCLUSIONS

The trial demonstrated that, even amongst the severely impaired stroke population, there could be improvement in motor performance in the sub-acute phase after stroke. The relationship between the improvement and the use of the robotic device is harder to evaluate and the results do not disprove the null hypothesis that there would be no difference between the groups as measured by the battery of outcome measures. Only one measure the ABILHAND found that the intervention group improved more significantly than those of the control group. *Post hoc* analysis of the FMA score most suggests that there was no real correlation between arm severity and improvement with the robot, however severe arm impairment did seem to respond to using the device. Limitations of the study related to the small population size, sensitivity of the outcome measures to assess change within this population; small proportion of those eligible participating in the trial; timing of the outcome measures; timing of the treatment; and the absence of a complete record of conventional therapy.

The implications of this trial will be considered more fully in Chapter Nine.

CHAPTER 7: A QUALITATIVE STUDY: USING INTERVIEWS TO EXPLORE PARTICIPANTS AND CARERS VIEWS OF USING THE REACHMAN DEVICE.

7.1 INTRODUCTION

Chapter six describes how the exploratory trial was undertaken and completed. It reports the findings from the study in terms of the clinical outcome measures and PROMS collected. However, it was felt to be important that participants and their carers perceptions of using the robotic device were also described. Therefore, a qualitative approach was used to explore participant's views of the impact of using the ReachMAN robot. This chapter describes the interview processes used and explores the experiences of eight of the participants in the exploratory trial and two carers.

7.2 BACKGROUND

Chapter Two described the literature that has looked at patient perceptions of the use of robotic devices (summary of the studies performed was also given in Table 2.2). This literature has shown that robotics are acceptable and appear safe to patients. However, there is a lack of in-depth and structured information on users' perspectives of using robotic devices for rehabilitation of their upper limb. Existing research on user perceptions of the use of robotic devices in upper limb rehabilitation is limited to a few studies of either patients^{195,224} or therapists²³¹, or both²²⁶. In these studies the scope of response is often predetermined by the use of closed questionnaires or Likert Scales. Furthermore, it has not always been made clear how the questionnaire was developed or administered, leading to possible bias. In some of the studies the questions or statements used were often unpublished and frequently there were no clear tables of results.

One recent publication has tried to address this gap. Hughes et al (2011)²²⁷ conducted a study on five participants who had upper limb problems six months or more post-stroke. Each subject used a novel robotic device. Following a six week trial, a purpose designed set of questions was developed and individual interviews were conducted. This found that participants had a positive response to the system, and provided feedback regarding the novel devices' service, function and effectiveness. Overall participants expressed they would have liked a home-based system targeting their whole arm. This study is the first that has explored more in depth views of people with stroke perceptions of

using a robotic device in upper limb rehabilitation. However the study was limited by its small study population. Furthermore interviews were very structured in nature, consisting of a questionnaire which included Likert questions, with only limited opportunities for the subjects to express in depth their views of the device. The authors acknowledge this limitation, and also acknowledge that a further limitation with the closed nature of their interview structure meant that the formation of the broader issues which may affect how people with a stroke may perceive robots in their rehabilitation could not be addressed.

For robotic aids to be effective, their design and protocols for use must be driven by clinical need and developed as a result of engagement with all interested parties: engineers, therapists, patients and their carers ²¹⁰. Ultimately, it is the interaction of the patient and carer with the robotic aid that will determine the regular use of and hence the effectiveness of robotic devices as a rehabilitative intervention ¹⁶⁹. Understanding the users perspective is essential to ensure that future devices will be acceptable, relevant and accessible¹³². It was therefore felt to be important that participants and their carers perceptions of using the robotic device were explored.

Establishing the opinion of a stroke patient may be challenging in the presence of expressive language problems and cognitive impairments. However, the carer's perspective may not be taken as a substitute for the patient's own opinions. Proxy interviewing risks discrepancies between the conclusions of the patient and carer and the failure of the proxy to predict or interpret the patient's preferences accurately³³¹. Lloyd et al (2006)³³¹ also express that the only way to effectively capture the patient's perspective is through direct questioning, providing support as necessary. Therefore, the aim of soliciting the carer's perspective was to capture their experiences and observations of the use of robotic devices as distinct from, and complementary to, the experiences of the patient.

7.3 CHOICE OF RESEARCH METHODOLOGY

To gain this understanding of both participants and carers views of using robotic devices as part of upper limb rehabilitation, it was felt that a qualitative methodology would be the most appropriate in this part of the study. Health researchers are increasingly using designs that combine qualitative and quantitative methods,³³² and this is often called mixed methods research. It was felt that by using both qualitative and quantitative methods in

these studies a more complete picture could be gained

Holt et al (2007)¹³⁴ echo this view commenting that qualitative research into the perceived benefits and barriers into the use of robotic devices in upper limb rehabilitation is required to inform the design and development of these devices. Furthermore, Coote and Stokes (2003)²²⁴ suggest that examination of user attitudes is essential to aid the translation of using robotic devices from the research environment to clinical practice. The National Institute for Health Research (2010)⁵ comment that involving users in the research process leads to research that meets their needs, is more reliable and is more likely to be put into practice

7.3.2 STUDY AIMS AND OBJECTIVES

Amid unanswered questions remaining over stroke survivors opinions of using robotic devices as a rehabilitation tool, and with the overriding aim of this thesis in mind (which was to bridge the gap between research into robotic devices and clinical practice) The aims of this study were to:

Aim:

To explore patients' perceptions of using a robotic aid for upper limb rehabilitation after acute stroke, in order to inform future robotic design and treatment protocols

Objectives:

Subjects were explained that the aim of the study was to find out how they felt about using The ReachMan device as part of their rehabilitation. In particular the aim was to find out their views and experience on using the device itself.

7.3.3 SELECTION OF QUALITATIVE RESEARCH APPROACHES

There are several approaches to qualitative research including, ethnography, action research, grounded theory and phenomenology ³³³. Each approach offers unique perspectives, which were all considered when choosing the most appropriate qualitative research design to address the aims of the study.

Ethnography is concerned with the study of a culture or subculture ³³³. Large-scale macro-ethnographies examine a large culture with its institutions, communities and value systems. Small scale micro-ethnographies investigate a single social setting such as a ward or small group of people ³³³. Data collection involves immersion in the setting by means of participant observation ³³⁴.

Action research aims to interpret and explain social situations while executing a change intervention aimed at improvement and involvement ³³⁴. This approach is problem-focused, context specific and future orientated ²⁴². Action research is a group activity based on a partnership between action researchers and participants whom are involved in the change process ^{334 333}.

Grounded theory (as developed by Glaser, Strauss, Corbin and their co-workers) is an attempt to develop a set of strategies for conducting rigorous qualitative research. It uses inductive strategies for analysing data. The researcher begins with no pre-existing theory, hypothesis, or expectation of findings but rather permits a theory to emerge directly from the data – that is, the theory is grounded in the data. The aim of the approach is not only to describe well the topic of study but also to develop adequate theoretical conceptualisations of findings.

The phenomenological approach allows in-depth exploration and interpretation of the experience of a phenomenon through an intensive study of individual cases of a small sample of people. This approach emphasises the value of describing and interpreting human experience, using descriptions and /or interpretations of everyday experiences as sources of data ³³⁵.

Ethnography was rejected as a method as it is only appropriate when addressing the experience of groups, cultures and subcultures with prolonged engagement and immersion in the setting under study.

Action research is a cyclic process in which research, action and evaluation are interlinked; involving change management and collaboration with participants ²⁴². This would be challenging in the context of the research question and research studies.

Ground Theory was also rejected as a method, as this methodology premise is focused on producing a new theory, and this was not felt to be the main focus of this study but rather to evaluate and gain an in depth understanding of subjects perspectives of using robotics in their arm rehabilitation

Phenomenology also did not quite fit the model to explore the aims required, as it aims to provide rich detail of lived experience of small numbers, narrative knowledge and an interpretation of human experience ^{335 333}

7.3.4 FRAMEWORK ANALYSIS

After careful consideration of the different types of methodology, it was decided to use Framework Analysis Method for this study.(developed by the National Centre for Social Research and described by Ritchie and Spencer (1994)³³⁶.

Framework Analysis is a thematic content analysis method that involves summarising and classifying data using a thematic framework ³³⁶.Framework Analysis is actually by definition a method of data analysis rather than a research paradigm such as ethnography, phenomenology, or grounded theory³³⁷, It has been noted to fit into a thematic methodology ³³⁸.

There was a number of reason why Framework Analysis was chosen: Firstly, In its theoretical commitment, this research is both interpretive and phenomenological. It seeks to make sense of the participants' experience, explores a concept from the perspective of the participant and acknowledges that each person's experience of the world is different and there is no one 'true experience' of the world ³³⁹ It is Heideggerian in that it seeks to understand the way people give meaning to experience of being-in-the-world and acknowledges that while each person shares being, their experience of being is always different ³⁴⁰ The use of Framework Analysis allowed both these elements to be address. However, unlike entirely inductive and iterative approaches such as grounded theory, Framework Analysis may be shaped by existing ideas and is

less focused on producing a new theory³³⁷, which also fitted well with the concepts of this study.

Furthermore, Framework Analysis has a well-defined method of synthesising and interpreting qualitative data which makes it an accessible analytic tool for a novice researcher³³⁶ such as the researchers performing this study. This systematic and sequential process provides a trail of evidence and hence enhances the dependability, consistency and conformity of the data³⁴¹.

7.3.5 DATA COLLECTION METHOD

Quantitative methods such as questionnaires have previously been used to measure patient attitudes towards rehabilitation robotics^{162 195 224 134 216 226 225}. However, this approach was considered inappropriate as the data generated from questionnaires lack depth and detail and is insufficient when exploring the complexity of factors that shape personal opinions and experiences. Furthermore, predetermined questions limit the opportunity for participants to discuss aspects of their experience that fall outside the remit of the questionnaire²⁴².

Semi-structured interviews were chosen as the data collection method as they are effective in gaining the participant's detailed views and experiences of a particular topic or phenomenon²⁴². Interviews should provide sufficient richness of data to analyse the insights and narratives of the individual participants. In a semi-structured interview the researcher sets the agenda in terms of the topics covered, but the participant's responses determine the amount and type of information provided about those topics and their relative importance³³⁴. The participant shares control over the conversation which allows for expansion on the topics most salient and preserves the ability for the participant to foreground issues personally relevant to them³⁴². The fluid two-way communication structure allows the researcher to clarify responses, prompt elaboration and probe further in areas of particular relevance to the research objectives³³⁴. Semi-structured interviews also allow a forum for the researcher to be attentive to a participant's beliefs and perspectives and how they may affect their health behaviours³³⁴. This balance of flexibility and structure best fitted the research aims of exploring the participants' perceptions of rehabilitation robotics.

Semi-structured interviews were favoured over open in-depth interviews as the research question was very focused around rehabilitation robotics rather than the total experience of stroke rehabilitation. Semi-structured interviews were preferred to focus groups because the experience of stroke rehabilitation is intensely personal and dependent on one's level of impairment, which makes group comparisons less useful. Furthermore, cognitive and language impairments affect group dynamics and the participants finished their robotic intervention at different times, making focus groups logistically difficult.

7.3.6 INTERVIEW TOPIC GUIDE

The interview topic guide (see Appendix V111) was based on the study's aims and objectives and also reflected questions posed in previously published research ^{134;231}. A pilot interview was carried out with a stroke patient who had used an earlier prototype of the robotic aid to explore areas to generate possible topics and gain experience in interview technique. The topic guide included the following: expectations of the robotic aid; benefits of robotics; acceptability of treatment protocol; design of the robot; use of robotics to enhance motivation; and opinion of having a robotic device at home. The topic guide was not intended to provide a rigid structure for the interview as the priority was to allow the participant to express their opinions and experiences freely. Rather, it was used as a prompt to focus the data collection and ensure that all relevant topic areas were explored during the interview.

7.3.7 ESTABLISHING RIGOUR IN THE STUDY

A number of strategies were used to improve the rigour of the study. This included detailed description of the process and the context in which the data was gathered both in the methodology and in reflective memoing. Participants were questioned during the interview process to clarify any points that were unclear to validate information. Analysis of the transcripts by a second researcher was used to validate the results gained. A reflective memo diary was used during the data analysis to show transparency

During this study the researcher developed reflexivity acknowledging the role of the researcher and the researchers' professional experiences, in the research process, from design, data collection and analysis through to completion.

7.3.8 RECRUITMENT

Following the robotic intervention, described in the previous chapter, all participants were invited to be interviewed by a physiotherapist to explore their experiences of using the robot. An independent physiotherapist (BS), who had had no involvement with the intervention, was chosen to complete the interviews to encourage honesty in the responses. The analysis was undertaken by the primary researcher and research team. Ethical approval for this stage of the study was obtained from the joint research ethics committee of the NHNN and the ION. All participants signed a consent form (see Appendix V11).

7.3.9 SETTING

Once the intervention phase has ceased, participants were contacted in person (usually in the rehabilitation unit where the participant was still ongoing rehabilitation) or by phone (if they had gone home) to ask if they would be willing to be interviewed. The interviews were carried out at a time and place convenient to the participants. Most participants chose to carry out the interview in the rehabilitation unit immediately prior to discharge. Three participants were interviewed at home. Although the researcher attempted to ensure a quiet, relaxed environment for all interviews, one participant chose to use a communal recreation room, which resulted in background noise and disturbances.

7.3.10 PARTICIPANTS

Eight out of 18 people who participated in the exploratory trial reported in chapter six were recruited to the interview stage, and two carers participated. The interviews were carried out in 2010, unfortunately the physiotherapist performing the interviews was unable to perform any further interviews with participants recruited in 2011/2012. Of the 13 people recruited into the exploratory trial, intervention arm during that time period two people

refused to be interviewed; and one had not yet finished the intervention arm preventing participation. The participants who agreed to be interviewed, all were early post stroke suffered either haemorrhagic or ischemic strokes ranging from two weeks to six weeks prior to recruitment to the study; three had a hemiparesis of the right side and five of the left side. Participant ages ranged from 25 to 78 with a mean age of 55 years. Participant characteristics are summarised in Table 7.1

Table 7.1: Characteristics of participants who were interviewed:

ID	Gender	Occupation	Age	Location of Stroke	Affected UL	Location of Interview	Time started intervention
P1	Female	Occupational Therapist	60	Right MCA Infarct	Left	NHNN	6 weeks
P2	Female	Retired Secretary	72	Right Lacunar	Left	Home	1 week
P3	Male	Retired Admiral	78	Right Lacunar	Left	NHNN	3 week
P4	Male	Unemployed	28	Left ICH	Right	NHNN	4 week
P5	Female	Full-time mother	39	Left MCA Infarct	Right	NHNN	4 week
P6	Male	Floor layer	25	Left subcortical	Right	NHNN	4 weeks
P7	Female	Housewife	37	Right MCA infarct	Left	Home	4 weeks
P8	Female	Unemployed	39	Right ACA	Left	NHNN	6 weeks
Carers							

Two participants P6 and P5 had language impairments. Individuals with language impairments are often excluded from qualitative studies in favor of the most verbally articulate ³³¹. However it was felt to be important to include participants with language impairments. This was to allow a more comprehensive perspective of individuals to be noted. A number of strategies were employed when interviewing patients with receptive and expressive dysphasia ³³¹. These included identifying communication strengths and strategies in advance with the participant and their speech and language therapist, the use of mainly closed questions to facilitate expression, and incorporating written communication to aid comprehension. The resultant limitations in the richness of the data were considered an acceptable compromise when compared with the alternative of excluding these participants from the research.

7.3.11 INTERVIEWS

Interviews were conducted by the interviewer (BS) on average a week after stopping using the robotic device. The interviewer was not involved in the delivery of the intervention and the interviews were conducted away from the device to reassure participants that they did not have to report favourably on the intervention. All interviews were tape recorded. Each interview covered the same general topics, although the participant was free to structure the conversation within each topic. Guiding questions were developed by the interviewer, the primary researcher (KB) and the primary investigator (DP) of the whole study.

7.3 12 ANALYSIS

Interviews were transcribed verbatim. The analysis was undertaken primarily by the primary researcher and the interviewer. The interview data were analysed using the Framework Analysis. Framework involves six stages: 1) identifying initial themes, 2) labeling the data, 3) sorting the data by theme, 4) synthesizing the data, 5) developing descriptive accounts and 6) exploring explanatory accounts. First, recurring themes were identified and developed. Then the themes were grouped into a number of main and sub-themes. At this stage an initial thematic framework was created. Labels were then attached to each section of the transcripts which is called indexing; the labels represented the theme to which it was associated. The thematic framework was then further developed to add any new themes. The next step was sorting the data by theme where sections of data with the same label were brought together. Charts were then created for each of the main themes using the context and language found in the data. The entire transcripts were also reread regularly to minimize fragmentation. The nature and content of each theme was described and discussed between the researchers. Explanation of links between themes were developed and further discussed. (Appendix VIV shows an example of this process).

NVivo 8 qualitative data analysis software was used to help organise the data during the indexing and charting stages and this facilitated collation of data under the identified themes. The use of computer aided qualitative data analysis software such as NVivo 8 was not intended to replace the researcher's data analysis but was used to organise the data in a systematic way, while maintaining the integrity of the original transcripts ²⁴²

7.4 RESULTS

The results are presented as the themes that emerged from the data. Quotes are used to support and illustrate points. The main themes identified were:

1. Impressions of the robot
2. Impact on symptoms and arm movement
3. Progress, Challenge and Encouragement
4. Fatigue
5. Use of the robot

The results will be described within these five themes where applicable (Table 7.2).

Table 7.2: Themes and subthemes from the interviews

Themes	Subthemes
Impression of the robot	Initial impressions
	Use of technology
Impact on symptoms and movement	Pain
	Physical Gain
	Confidence/ use of arm
	Enjoyment
Progress, Challenge and Encouragement	Making Progress
	Maintaining Progress
	Challenge
Fatigue	Physical tiredness
	Cognitive tiredness
Practical Use of the robot	Independent use

7.4.1 IMPRESSION OF THE ROBOT.

INITIAL IMPRESSIONS

On initial use of the robot, some participants expressed some fear and doubts on initially encountering the robot:

“I had mixed feelings about that really. I was a bit dubious of it.” (P4)

However, these fears were not long-lasting and dissipated as the participants got used to the robot:

“Well, first impression, I was *frightened* of it. [...] Because I hadn’t been on anything like that before [...] but by the time I’d taken my last little session on it, I was absolutely thrilled with it! *Very* impressed with it. Loved it!” (P2).

“I did not realise how it will work....but then I realised what and how it was going to help me and where it was running. “ (P8)

They were concerned that these first impressions may worry other users:

“I think that some people might find it a bit more intimidating, but it’s not, I didn’t think...I thought it was ...Once you got used to it and you realised what you could do with it...then it was good.” (P1)

None of the participants were worried about the safety of the device:

“I felt safe all the time... Yeah it’s safe. Again, I had no issues like that, not at all, got no issues like that.” (P4)

TECHNOLOGY

Participants expressed a variety of opinions of using technology in their upper limb rehabilitation. Some participants found using the device as a novelty:

“To be introduced to this kind of device is a thrill in itself, of course it is!” and “Well, it showed was that the therapy was in the 21st century as opposed to the 19th century!” (P3)

P4 felt that having computer games or virtual reality technology would help to stimulate stroke patients both cognitively and physically:

“Both would be good for you. [...] And at the same time your brain’s getting stimulated with the games [...] and then virtual reality is using your arms to pick up, to pretend you’re picking up things. So, in both ways... it’s helping you in both ways.” (P4)

Participants also made general comments about ReachMAN itself. They did not report any problems with understanding the graphics and following the desired movements, but the sensitivity of the graphical feedback from the finger and wrist movements was confusing for one of the participants:

“The other motions were not nearly so clear as to whether you had scored or whether you hadn’t scored[...] I think they need some more work them to make them more precise. [...] So you can tell, what is the result of your effort – visually tell”. (P3)

The participants were generally positive about incorporating computer games into the robot. Computer games were suggested as a means to challenge and engage stroke patients:

“a good idea, probably quite a good idea, that you could challenge yourself a bit more on it. [...] I think that if you were winning something you would probably want to keep on doing it.” (P1)

The older participant expressed they were happy with the current robot and liked its simplicity

“Ah, no I mean you just want the basic, the most basic functions to help exercise the hand endlessly, like the robot [...] in the right and proper manner to get it back to life.”(p2)

While the younger participants would have been happy for the machine to have been more 'high tech'

"There could be a bit more to look at, a bit more to be, you know, even could maybe possibly use creatures, like little creatures running around and trying to get them. You know, stuff like that... make it a bit more high tech "(p4)

7.4.2 IMPACT ON SYMPTOMS AND MOVEMENT

Participants reported a variety of impacts on their arm symptoms and arm movement with using the robot. These are grouped into subthemes: pain, physical and functional gains, confidence, enjoyment.

PAIN

Although only two participants (P5 and P6) spoke about experiencing arm pain as a result of using the robot, in one participant his experience of pain was such that it prevented him from continuing to use ReachMAN. Both of these participants had significant expressive language impairments, and could only express their experience in response to closed questions.

BS: I think I understand but **[P5: Yeah]** I'm going to say it again **[P5: Yeah]** to check with you, I don't want to pick things up wrong from you so...Once you took your hand *out* of the robot, having used it, it would be stiff and painful?

P5: Yes. Yeah.

P5 directly attributed his arm pain to the robot, as explained by P6's carer:

"he wasn't *over* keen on it because it *caused* a pain in his shoulder [...] But since he's not been doing it, he's got a lot better, so it obviously was aggravating what was there" (C6)

However other participants also discussed pain that they had in their arms and expressed that felt that the using the robot eased pain and stiffness they were experiencing:

"My fingers were stiff at the beginning. I found it hard to press with my finger. Gradually I found it easier...stiffness and pain got easier" (P7)

PHYSICAL GAIN

In contrast to the pain experienced by two of the participants, the remaining six participants clearly articulated the gains and benefits they obtained from using the robot. Positive language was used to describe this. The participants spoke about improved arm movement and better ability to carry out different functional tasks following using the robot, in particular, improvements in grip strength and the ability to pick up objects:

“it was after using it that I was able to start picking up bottles and things [...] Also when I first used it I moved my... started to move my... arm around a lot... and grip which I couldn’t do before.” (P1)

Another subject described that improved hand movement resulted in better performance of activities such as, holding a cup and opening a door:

“Yes my hand is much better... I can hold papers, book, a cup and it is easier to open doors” (p7)

Furthermore, P4 felt that the robot helped to relax his hand:

“It’s made my hand more relaxed and made my hand work more.”

Improved physical appearance was also mentioned by the participants as a benefit of using the robot.

C3 mentioned how the robot “stops that awful claw-like arrangement, that you’re stuck with after a stroke” and P2 describes how her arm “not only felt stronger, it *looked* stronger.”

CONFIDENCE

A number of participants spoke about how physical improvements in their UL led to improved confidence. P1 described how improved UL function enhanced her ability to cope with having a stroke:

“I think, I think that when you’ve had a stroke, you just don’t know how much...all the problems are...Ahm... and what I found was that this, the more I can do with

this hand, because it *will* hold things...the more, the more it makes you feel more confident in actually *managing* your stroke.”

P3 describes how this confidence is directly related to the effectiveness of the intervention:

“You really gain a great deal of confidence in some piece of kit or some exercises if they *actually* do make a difference [...] but if there is no sign of that, then it will quickly... confidence will fall.”

ENJOYMENT:

The participants spoke about the enjoyment or pleasure they got from using the robot. P2, in particular, was very vocal about enjoying RMT and taking part in the research process:

“Well, I...if, given the chance I'd have gone on it everyday. I really would, cos I enjoyed it. When I knew, you know, anticipation of knowing I was going down was great and I used to swank a bit really, you know. They'd say 'are you gonna come and, you know, do this?' and I'd say 'Sorry, I'm going to help the... University about the, you know, about the robot arm' [...] I was *delighted* to do it!”

7.4.3 PROGRESS, CHALLENGE AND ENCOURAGEMENT

An overriding theme used in almost every interview was participants speaking about their progress and the encouragement they took from reflecting on their development and rising to the challenge of the robot. These concepts were inextricably linked in the participants' dialogue and are therefore combined here to form one theme.

MAKING PROGRESS

Making progress in their recovery was a common theme expressed by the participants. Progress was expressed as a positive and pressing concept: “*a/ways* urgent to make progress” (C3) and “anything that's gonna help progress then is good” (C6). Lack of progress was experienced as disappointment and self blame to some extent, as evidenced in these statements by P3:

“I'm just disappointed that I... with *myself* that I didn't make greater progress.”

“But of course that doesn’t quite work out like that... And the great thing is not necessarily to blame the robot, is you blame yourself or blame the illness or whatever it is.”

The expectation that the robot could help progression of UL recovery was described along a continuum from hope to certainty. Comments from P3 and C3 depict this range of opinion:

“Well I *hoped* that it would [help]. Confident, one can’t really say that, because you just don’t know, you haven’t a clue... but you could lay a hope, that it was certainly going to contribute.” (P3)

“It was obvious, it was obvious that it was something that would help! [...] I mean, not *tomorrow*, *but*, you know it would *start* the process of helping, yeah.” (C3)

MONITORING PROGRESS

The robot was not seen as encouraging in itself:

“I can’t really say how much it either encouraged me or discouraged me. It didn’t do either really.” (P3)

Instead it was the feedback from the robot that allowed the participants to monitor their progress, that was found to be encouraging. P3 explains how the robot was sensitive enough to perceive movement that a therapist may not be able to detect:

“it measured some movement in the muscles which was not otherwise evident in terms of ‘here’s your hand’, and it didn’t shift one iota. But the fact is, the robot measured that it was trying [...] and that was encouraging.”

The participants described monitoring their progress as they advanced through the difficulty levels and achieved better scores on the robot:

“Yeah. I’ve progressed...I can tell I’ve progressed cos I started on level one and now I’m on level eight[...] I’m at 100% on level eight...So, you know, that’s progress!” (P4)

They described how achieving this progress was experienced as encouraging:

“And when you’d sorta mastered that one, and it was, you had high numbers again. You know, you feel quite proud of yourself, you know, it lifts, lifts your spirit.” (P2)

CHALLENGE:

Progressing through the difficulty levels gave the participants something to aim for and encouraged them to continue to challenge themselves:

“When he puts it up a notch and it goes from 1 to 2 or up to 7 or 8, I think it was in this, Ahm, that was a clear distinction between one level and the next, and that was jolly good. Cos it gave you something to aim at, once you got going on it, but you had to get going on it. [...] so that was well designed.” (P3)

The ability to monitor their progress and the challenge to constantly improve their scores was seen as an element of competition:

“No. You could see it. It was visual. The feedback that you were getting was there, for you to see [BS:Yeah] itself you know. It couldn’t have added any more to it. [BS:Mhmm]And ahm.. no that was very satisfying what you could see on the screen. You could see you were progressing, and maybe *beating* the computer a little bit sometimes! It was like a little bit of a *competition* going on!”

One participant (P4) had progressed to the most difficult level and felt that the robot no longer challenged him sufficiently. He wanted to add extra levels:

“Probably four or five weeks I’ve been on here and I’ve hit level 8 and got the 100% and now [...] I said, ‘what’s the next level?’ He said ‘there’s not a next level’. So I was like, well I’ve hit the challenge. [...] So, ‘what happens now then?’”

7.4.4 FATIGUE

The issue of fatigue frequently arose during the interviews, with all participants and carers mentioning this with relation to using the device. The participants discussed the mental and physical effort required for rehabilitation and the tiredness they felt as a result. The participants spontaneously described the robot as a device that required both cognitive and physical effort:

“You really have to use your brain. You have to *think* about it. It’s a *two*-sided thing this really. You really do have to use your thinking and you do have to use your *own arm*.” (P2)

The tiredness described by the participants was both physical and mental. P3 illustrated how this fatigue was an unexpected feature of stroke rehabilitation:

“what one doesn’t realize for a stroke situation, what one doesn’t realize, is how much effort you need to put into the whole process of working on rehabilitation and how tiring that is. And it’s not just physical tiring; it’s mental tiring, as much as physical tiring.”

Tiredness impacted on how long the participants were able to use the robot for in one session. P4 explained that using the robot for a half an hour session was too long due to physical fatigue:

“You’d be tired, you’d be physically shattered by the end of it. I’d still say that, and I’m getting better quicker, quick and I’m finding it tired [...] and I’m only young.”

He suggested that 10 or 15 minutes was the optimal length time to use the robot for in one session. C3 described the general fatigue in the acute period following stroke and suggested gradually building up the frequency to assist with fatigue management:

“I think, once a day, certainly when you begin, because you’re so tired [...] but *maybe*, you know, when you’re getting fitter, and ahm more into your physiotherapy and better, then morning and afternoon would be even better.”

P1 described her difficulty maintaining concentration whilst using the robot and how she quickly she got distracted when she was tired:

“I think that after a while I used to start... one is I got distracted, so if I got distracted I didn’t always follow [...] what was happening. The other thing is, is that I found sometimes after a while just looking at the, the program itself [...] I started to get a bit sleepy or started to get a bit distracted and starting, starting to close my eyes... when I was watching it.”

Only one participant wanted to use the robot for longer periods than prescribed. P2 recalled being on the robot for up to an hour. Tiredness was not an issue for her, she was not concerned about fatigue, unlike her therapists:

“They worried more about me getting tired than I did [...] I was enjoying it too much!”

The two carers also commented how tired their family member appeared to be after using the robot:

“his arm tired quickly,... he was so tired... couldn't use the machine for long” (C3)

7.4.5 PRACTICAL USE OF THE ROBOT

INDEPENDENT USE

The participants' express a desire to carry out using the robotic device on their own outside therapy hours and they barriers they identified to being able to do it. The participants expressed frustration at the lack of opportunities available to continue upper limb therapy outside of structured therapy time. They believed that the robot could provide this type of therapy:

“One of the frustrating things about the hospital, even at Queen Square, we always thought, some of us, was that you couldn't do things at the weekend! [...] Saturday and Sunday was wasted! Or very largely wasted. There were *some* things that were set up 'specially [...] But for, for the most part, it was wasted time, you could have been doing something like this for example.” (P3)

They spoke more specifically of their frustration at the fact that they could not use the robot independently:

“that's what irritates me, that I can't use it when I want. [...] So I have to, it *frustrates* me cos it should be in the corner of the gym where you go in there and do it all yourself, put your arm in there and then it'd be good.” (P7)

The main barrier to independent use of the robot was that the participants were not able to set themselves up in the robot:

“One of the problems is that you can only do it whilst you’ve got people with you, when you’ve got the technician and somebody with you.” (P1).

Problems with the physical hand-robot interface and the complexity of the computer interface were identified as the main issues. The difficulty of getting a weak arm positioned into the robot was described by the participants and they suggested that the link between the hand and the robot could be redesigned to make this easier:

“I suppose if you had, if you actually had...ahm. Sort of a, sort of a stick or something like that that you could position your hand onto...then that would be, that would be possible. You’d need someone, or someone who had one- functional arms, in order to set it up.” (P8)

P4 did not believe that he had the computer skills to navigate the software used to run the robot:

“ you need to set up and it looks very complicated to set up and you need them to do it”

He suggested that a touch screen interface, which would automatically load the robot computer program, would make it simpler and more accessible to patients:

“You’d go in there, touch the screen, touch the screen, to work it out, so it does it all there for you” (P4)

7.6 DISCUSSION

The objectives of this study were to understand participants’ experiences of using the ReachMan device, and using a robotic device as part of their arm rehabilitation, and to gain greater insight as to how the system might be improved in the future

The interviews found that participants expressed generally that they enjoyed using the robotic device and were mostly very positive about using the device, provided that it did not cause pain or stiffness (one participant stopped using ReachMan due to shoulder pain). With the exception of this one participant, all the others attributed improvement in

their arm movements with the use of the robot and the primary focus in all was improvement. These findings support previous research in that the majority of stroke patients are positively disposed to using robotics for upper limb rehabilitation^{162;195;224;216;226;134; 225}. The participants were initially cautious about the robot and reported needing to get used to it. In previous studies, therapists cited safety issues and appearance as a concern^{224;231;134}. None of the participants in this study reported concerns about safety. Neither did appearance of the robot itself emerge as a theme, with participants expressing more concern with the effectiveness and usability of the device.

7.6.1 PERCEIVED BENEFITS OF USING THE ROBOT

A principal theme of the interviews was the positive language used by the participants when describing their thoughts of using the robotic device. They described both physical and psychosocial gains arising from using the machine. Participants reported improved confidence, enjoyment, better appearance of the hand and improved performance in functional activities. Prior research studies have also shown that stroke patients find robotics helpful and beneficial, and are content with the results from using robotic devices but do not expand on what aspects of the robot patients find beneficial. The participants in Coote and Stokes(2003)²²⁴ mention improved stiffness and ability to perform activities but further detail is not provided. Participants questioned in study by Hughes et al (2010)²²⁷ also describe improvements in arm and hand function.

This interview study design enabled participants to expand on the gains they perceived they had made from using the device. They described that improved hand movement resulted in better performance of activities such as picking up a bottle, holding a cup and opening a door. Achievement of these specific markers of independence signifies a return to valued activities, which has been postulated to be key to stroke patients' definition of recovery¹³². The participants attributed their improved functional ability directly to using the robot.

This perceived gain however was not captured in the clinical rated objective outcome measures, reported in Chapter Six, although a patient reported measure (the ABILHAND) did show statically significant change. Results from the clinical study did show that trends suggesting arm improvement with the clinical measures. The finding of perceived improvement in function in their arms, suggested the value in using interviews and

questioning participants, as this strengthens the findings and trends suggested by the more general outcome measures used.

It must however be noted that the proportion of motor recovery attributable to using ReachMAN in these participants cannot be quantified to the use of the robot alone, as participants were also simultaneously engaged in intensive MDT rehabilitation and were also in the subacute post-stroke period where the most spontaneous recovery occurs ¹⁰⁹.

Participants reported improved confidence which may indicate better self-efficacy. This is the confidence in one's ability to carry out a behavior or task ³⁴³. Improved self-efficacy has been linked to enhanced participation in rehabilitation, leading to better functional outcome ³⁴⁴.

Participants expressed enjoyment in using the robotic device, however part of the enjoyment experienced appeared to derive from participating in the research project. One participant in particular was very proud of her contribution and attained a certain social status on the ward by being involved in the project (P2). The same enthusiasm may not be shown if using a robotic device is introduced as a standard therapeutic adjunct, which may adversely affect motivation to use it. Therefore, it is possible that an element of the Hawthorne effect occurred, where the participants are merely reporting more benefit due to being involved in the study.

7.6.2 PAIN AND STIFFNESS

In previous studies, the effect of using robotic device on patient's experience of pain and stiffness was minimal. Coote and Stokes (2003) ²²⁴ reported no effect of using GENTLE/s device on pre-existing pain in two patients and Colombo et al (2007) ²¹⁶ reported low scores on the pain subscale of the IMI which indicates no exacerbation of pain. In contrast, two out of the eight stroke patients in this study (P5 and P6) reported experiencing pain, which one (P5) related directly to the use of the robot and this participant ceased using the robot due to pain. Hale et al (2012) ³⁴⁵ also found similar reports of pain from subjects using a virtual reality device for upper limb rehabilitation.

The development of pain with the use of Reachman is a significant issue and one that was fully explored with the participant in question (as discussed in Chapter Six). Coskun et al (2013)³⁴⁶ highlighted the complexities of diagnosing the cause of shoulder pain post stroke, with many potential reasons which could cause this, including abnormal patterns of muscle activation. The fact that this participant did express pain that was directly attributed to use of the machine, highlights the need to be vigilant when participants use ReachMAN. This also reinforces the need that arm movements, with future use of the machine should be introduced with a gradual build up of duration and intensity. The actual movements that occur in the arm during the use of the robot should also be carefully examined (Both these strategies were employed in the clinical trial and in light of the pain experienced show that this would need to be continued in the future).

7.6.3 TIREDNESS AND ITS IMPLICATION FOR TREATMENT PROTOCOL

This study found that fatigue was a major issue for the participants and this impacted on their interaction with the robotic aid. The robotic sessions were scheduled to be as long as the participant wished to use the device. Most participants found robotic exercise to be both mentally and physically tiring and 20 minutes was seen to be the maximum duration that they could use the machine for. Frequent shorter sessions were preferred by the participants. To date, clinical trials of robotics have used intervention protocols of 30-60 minutes per day^{205;206 171} However, these trials were carried out in a chronic stroke population, with patients more than six months after stroke and already discharged from inpatient rehabilitation. The participants in this study commenced using the robot within six weeks of their stroke and were concurrently engaged in an intensive, multidisciplinary inpatient neurorehabilitation program. Doornebosch et al (2007)²²⁶ reported similar findings, where sub-acute patients used the robot in passive mode for 20 minutes or less if the therapist noticed that the patient appeared tired. The intensity of the rehabilitation combined with post-stroke fatigue and reduced endurance may have been contributing factors as to why participants were only able to tolerate using the robot for short periods. Fatigue is a very important factor to consider when developing a therapeutic intervention for acute stroke patients and further work is needed to investigate this further. However, the findings of these interviews suggest that frequent, short sessions are recommended.

This area and its implications for all phases of the research study will be discussed in Chapter Nine.

7.6.4 INDEPENDENT USE

The participant's desire to use the robotic aid independently was a strong theme throughout. The participants displayed frustration at not being able to do this independently due to the arm attachment and computer software. Participants were unable to switch on the programme independently to use the machine. The main physical barrier to independent use was the inability to place the paretic arm into the robot arm support independently. Previous studies have also reported difficulty with independent arm attachment^{226 224 134}. In light of the participants' desire to use Reachman independently, this represents a need for the machine to be redesigned. One participant suggested a touch-screen computer interface to facilitate the patients to initiate and control the device during a session. This design feature was successfully used in the ACRE 2 device²²⁶ and could be considered for the next model of the ReachMAN device. The ultimate goal of rehabilitation robotics is to facilitate supplementary independent practice²¹⁰, requiring assistance to set up the robotic aid was disappointing to the participants and limited the ability to perform this independent practice.

7.6.5 USE OF TECHNOLOGY IN REHABILITATION

All patients were generally positive about using a novel device as part of their upper limb rehabilitation. However, studies of technology use, attitudes, and abilities do show that older adults are less likely to use technology (as discussed in chapter one, a larger percentage of stroke patients are over 65) compared with younger adults and can be fearful of using technology³⁴⁷. The older participants in the interviews expressed no problem with using the machine after their initial impressions and were happy with the simple graphics used in the ReachMAN program. The younger participants however, did comment that they would have liked these graphics to have been more complicated. These are important areas to consider when looking at any design changes to the device. Further

piloting perhaps with some more complex graphics and games that retain their simplicity would assist in bridging this mismatch between the ages.

7.6.6 IMPLICATIONS OF THESE RESULTS

This is one of the first studies to have captured what is important to people with stroke when using a robotic device for upper limb rehabilitation. The study has also encapsulated how they felt their movement was changing in ways meaningful to them as individuals, and how the ReachMan device met their requirements.

The wider implications of these results (in combination with the previous literature) are that the use of robotic devices in general is acceptable and enjoyable, but that patients would like future rehabilitation robot systems to be designed that could be used at home independently. Participants wished to use the machine for only short periods throughout the day

7.7 WEAKNESSES AND LIMITATIONS IN THE STUDY

The generalisability of the study is limited by the small participant population. The interview data did not reach a level of saturation, as each consecutive interview continued to raise new issues. A larger, more diverse sample population would be required to address this.

The independent interviewer (BS) by her own admission was inexperienced and this was found to be apparent in the interview data. Some opportunities to probe for clarification or a further example were missed, and occasionally there was insufficient use of pauses to encourage the participant to expand on their previous comments²⁴². However, this improved as the researcher became more comfortable in her interviewer role.

It is acknowledged that some element of researcher influence is unavoidable in the interviews. However each interview was looked at by at least two (sometimes three) different people and were critically examined and all attempt to minimise the impact of biases, preconceptions and influences during data collection and analysis was made. The

interviewer was introduced to the participants as a physiotherapist, which may have opened the possibility of a social desirability bias whereby the participants may have presented a more positive experience of the robotic device to please the researcher.

It is well acknowledged that interviews only give access to what people say, not what they do³³⁴. In line with the interpretivist approach, no attempt was made to verify the participants comments to achieve a 'true story'³³⁴.

It is acknowledged that using a semi-structured interview rather than an open in-depth interview may have resulted in missing some of the broader experiences and perceptions participants had of using the robotic device. Furthermore participant's general experiences of having a stroke, having an UL impairment, participating in inpatient neurorehabilitation and expectations of rehabilitation and recovery following discharge were also missed.

7.7.1 TIMING OF INTERVIEWS:

Interviews were performed immediately prior to discharge in most cases, and this functioned to minimise recall bias, and allowed the experience of using the robot to be still fresh in the participants' minds. However, this time of transition is often fraught with anxiety, anticipation and worry as the stroke patients finish inpatient rehabilitation³⁴⁸ and return home with significant functional limitations. This may have impacted on the participant's engagement with the research process.

7.8 CONCLUSION

This chapter explores the qualitative experiences of eight participants and two carers of using the ReachMAN robotic device. The qualitative methodology used semi-structured interviews which were analysed using Framework Analysis. The interviews were performed in parallel with the quantitative study reported in Chapter Six. The main findings were that using the device was a positive experience, which participants enjoyed and they attributed physical gains in their arm function with its use, provided it does not cause pain. Crucially, participants found they could only use the device for short periods, as it was found to both be mentally and physically taxing. To avoid this participants suggested that

use of the device should be short and frequent. The opportunity to practice independently was important to the participants.

7.9 SUMMARY

This chapter has discussed the qualitative research study that was performed to investigate participants' perceptions of using the robotic device. The following chapter details a psychometric analysis of two of the outcome measures used in the study.

CHAPTER 8: PSYCHOMETRIC ANALYSIS OF THE MEASURES USED IN THE STUDY

8.1 INTRODUCTION

Chapters five, six and seven have detailed the research studies that were carried out to evaluate the use of robotic devices in upper limb rehabilitation. This chapter will discuss a comprehensive psychometric analysis that was completed on two of the outcome measures used in the studies, using the results from the studies performed.

8.2 BACKGROUND

There is a growing consensus that the conclusions made from neurologic studies are partially dependent on the rating scale used^{259 258}. Rating scales must therefore be clinically useful and scientifically sound. Clinical usefulness has been described as the successful incorporation of a measure into clinical practice and its appropriateness to the study sample²⁴⁵. Scientific soundness refers to the demonstration of reliable, valid and responsive measurement of the outcome of interest.²⁴⁵ In regard to upper limb recovery post stroke, Woodbury et al (2009)²⁸⁰ comment that there is a real need to ascertain whether assessment tools commonly used in research are accurately quantifying impairment and characterizing recovery.

A means to achieve this scientific soundness is to perform thorough psychometric evaluations of outcome measures and this is endorsed by FDA²⁴⁸, EMEA³⁴⁹ guidelines and MRC²³⁷ framework. Work by Hobart et al (2009)²⁵⁹ and others²⁸⁰ argue that use of traditional psychometric analysis alone to evaluate outcome scales is insufficient and can lead to weaknesses in scales being overlooked. The use of newer psychometric analysis (such as Rasch) can highlight strength and weakness of scales, which could otherwise go unseen.²⁴⁵

This Chapter will therefore describe the psychometric analysis, using new and traditional methods, that was carried out on the results, from two of the scales that were used in the studies- a patient reported outcome measure- DASH , and a clinician rated scale FMA

The use of Patient-reported outcomes (PRO) measures in stroke research is a relatively new development.²⁵⁴ Patient reported outcomes are patient-derived questionnaires that

measure any aspect of a patient's health status ranging from symptoms to other complex concepts such as quality of life, which is a multifaceted construct involving physical, psychological, and social components.³⁵⁰ Although there is a growing call to include participation measures in stroke research, as an important component of disability, few measures look at this aspect²⁵⁴. Specifically, few PRO measures scores have been found for the upper limb post stroke³⁵¹.

The Disabilities of the Arm, Shoulder and Hand (DASH) is a 30 item scale which measures everyday active function in the arm and is a 30-item, self-report rating scale developed for use in orthopaedic populations.³⁰⁰ It has been described as being the most widely used upper limb rating scale.³⁵² It has not been widely used in stroke populations^{214;351}. However due to the lack of PRO measures it was felt to be useful to evaluate the psychometric properties of the DASH in people with stroke to determine its suitability as an outcome measure in this population.

The Fugl- Meyer Assessment Score (upper limb section)²⁷² is the most widely used clinical outcome score of post stroke arm impairment²⁸⁰. It is widely used in stroke research to evaluate the success of novel upper limb interventions where it has been used as the primary outcome measure. The measure has also been extensively studied to examine its psychometric properties and it is often referred to as a “gold standard” measure with which other upper limb measures are compared to.

Newer (“modern”) psychometric analysis methods (such as using Rasch analysis) have been performed on the FMA upper limb score to examine the dimensionality and construct validity of the scale.²⁸⁰ However studies to compare and contrast traditional and newer psychometric analysis methods to evaluate the measure have not been performed.

The FMA measure consists of 33 items which are scored on a 3 point rating scale: 0=unable to perform, 1= partial ability to perform and 2= near normal ability to perform. The scores are then summed to produce a score of 66.

8.3 TRADITIONAL PSYCHOMETRIC ANALYSES

Traditional psychometric analysis is based upon correlational or descriptive analyses to evaluate scaling assumptions, reliability and validity. Usual traditional psychometric

analyses examines five psychometric properties³⁵³: data quality, scaling assumptions, acceptability, reliability (internal consistency), convergent and discriminant construct validity. These terms will now be defined:

Data quality

This is the extent to which an instrument can be used successfully in a clinical setting³⁵⁴. In the analysis used in this thesis, this was determined to be high if items had low missing data (<10%), and if a high percentage of scale scores were computable for each patient.

Scaling assumptions

This is the legitimacy to sum item scores without weighting or standardisation to generate a total score. In the psychometric analysis performed in this section the scores were examined by determining whether items in each scale had roughly similar response-option frequency distributions, equivalent mean and variances, and equivalent item-total correlations.^{353;354}

Acceptability

This is the targeting of a scale to a sample so that score distributions adequately represent the true distribution of health status in the sample^{353;354}. This was achieved by the scores being examined to determine that observed scores were well distributed,^{353;354} mean scores were near the scale mid-point^{353;354}, floor and ceiling effects were low, and skewness statistics ranged from -1 to +1.^{353;354}

Validity

Validity is an assessment of whether an instrument actually measures what it purports to measure. It can be broadly defined as the extent to which the instrument measures the concept it purports or is intended to measure^{355;356}. In this analysis measures construct validity was examined. This is examining the relation between the measure and other measures or behaviours^{240;355}. This is performed using convergent and discriminant construct validity.^{353;354} Correlations between scales were examined to determine the extent to which each instrument: 1) measures what it is supposed to measure (convergent

construct validity) and 2) does not measure what it is not designed to measure (discriminant construct validity).

Reliability

Reliability is an estimate of the reproducibility and internal consistency of an outcome measure³⁵⁶. A reliable measure is one which produces results that are accurate, consistent, stable over time, and reproducible. Internal consistency of a measure is usually evaluated when looking at the reliability of that measure^{353;354}. This is the extent to which items comprising a scale measure the same concept – that is measure of the homogeneity of the scale. In this evaluation this was examined using Cronbach's alpha coefficient.^{353;354} It is recommended that $\alpha > 0.80$.^{353;354}

“New” Psychometric analysis-Rasch Analysis

Rasch analysis allows the transformation of ordinal data to interval data. It assumes that the likelihood of any item being endorsed is based on item difficulty and person ability. Rasch analysis, therefore, is a probabilistic mathematic modelling technique used to assess properties of outcome measures. Where data are shown to accord with model expectations, the internal construct validity of the scale is supported, and a transformation of ordinal data to interval scaling is possible²⁵⁸. This helps to improve the accuracy with which to measure differences between people and clinical change. It has been argued that Rasch analysis has a greater potential to identify the merits of a rating scale than traditional psychometric methods²⁵⁸.

There is no agreed standard method to perform Rasch analysis. However Tennant and Conaghan (2007)³⁵⁷ outlined seven criteria with which a measure can be analysed against. This criteria has been used in studies investigated the psychometric properties of rating scales used in neurological populations³⁵⁸. These criteria were therefore used in the analysis for this thesis. There are specifically

1. *Item response-threshold ordering*. The threshold between two response options is the location, measured in logits, where the two options are equally likely. If correctly ordered, the threshold between response options 1 and 2 will occur at a more negative location than the threshold between options 2 and 3, for example. However, response options can be disordered, particularly for items with a higher number of response options, indicating

that the extra response options do not provide additional information about a person's true location on the variable that the item represents. In such instances, Rasch analysis can be used to reduce the number of response options by combining two or more options into a single option. . An example of this can be seen in the Functional Independence Measure. An item on this measure asks raters to rate whether an individual is able to manage their bladder .There is a rating of 50% dependence for assistance in bladder management, which is difficult to quantify. This can disorder the scoring and is best reduced to 0 independent, 1 needs some help, dependent.

2. Tests of fit to the model. This is the extent that observed data fits the Rasch model and this can be examined at both the scale and item level. At the scale level, summary item fit residuals are examined, which ideally should have a mean of zero and a standard deviation of 1 (a standard deviation of > 1.4 can indicate misfit at the individual item level), summary person fit residuals (where a high standard deviation can indicate individual participants who misfit the model and thus severely reduce the fit of the model to the data), as well as the chi-square for the item-trait interaction, which should be non-significant. At the item level, item fit residuals were examined, which should fall between ± 2.5 (overly positive residuals indicate that responses to an item do not fit the Rasch model; overly negative residuals indicate that an item shares so much variance with other items in the scale that the item provides very little additional information, and so is redundant, and item chi-square values, which should be non-significant ($p > .05$, Bonferonni adjusted).

To give an example to explain this clearer: Figure 8.1 illustrates the Rivermead mobility index. The ideal is that the Item response categories work in a logical manner to reflect a continuum of mobility i.e.- start with poor mobility, to gradually improve to good mobility via a series of steps (items) However, where a scale diverges from this, this is called a misfit. I.e ability to climb stairs does not necessary prevent someone being able to walk outdoors and these two items therefore misfitted. The stairs item could therefore be omitted from the scale.

3. Differential item functioning. This examines the extent to which items functioned differently by gender, age, ethnicity, marital status, number of days since the stroke, clinical diagnoses, and walking status., For example, men and women use different language so in a 'high stakes' language test (for example one that allows entrance to

university) women will outperform men if the language tested is around clothes, food and colour, and men will outperform women if the language is centered round fast cars

4. *Item locations.* The location on the Rasch continuum, measured in logits. Ideally, items will have locations that are evenly spaced over a wide range rather than being clustered at the same location. Also, ideally this range of item locations will adequately target the range of locations of the target population. Often this doesn't occur with change on an ordinal scale is 'easier' often in the mid point of the range. Hobart et al ²⁵⁸ demonstrates this in their paper on the use of Rasch analysis.

5. *Reliability.* The Person Separation Index (PSI) was used to assess reliability. This statistic can be considered equivalent to Cronbach's alpha, with values $\geq .70$ regarded as adequate.

6. *Local dependency.* High standardised residual correlations (SRCs) between two items indicate that the responses to these items covary to a greater extent than predicted by the Rasch model. This can indicate the presence of local dependency, where the response to one item is dependent on the response to another item. SRCs $> .3$ can indicate local dependency among items For example . Scales which measure mobility have items such as: A person can walk 500m, 50m, 5 m. However, if you can walk 500m you can walk 50 m and 5m so the answers to questions 2 and 3 are dependent on the answer to one.

7. *Unidimensionality.* An assumption of the Rasch model is that the items of a scale form a unidimensional variable, in other words a single construct. Unidimensionality of the final scales was tested using paired t-tests to compare person scores from the two most divergent subsets of items ²⁴¹. For this procedure, subsets were formed by selecting the items loading most positively and most negatively on the first factor extracted in a principle component analysis of residuals. If no more than 5% of t-tests are significant, or if more than 5% are significant but the lower confidence interval corresponds to less than 5%, the assumption of unidimensionality has not been violated.

Figure 8.1: Rivemead Mobility Index

Rivermead Mobility Index

Please tick 'No' or 'Yes' for each question

	No	Yes
1. Turning over in bed		
2. Lying to sitting	<input type="checkbox"/>	<input type="checkbox"/>
3. Sitting balance	<input type="checkbox"/>	<input type="checkbox"/>
4. Sitting to standing	<input type="checkbox"/>	<input type="checkbox"/>
5. Standing unsupported	<input type="checkbox"/>	<input type="checkbox"/>
6. Transfer	<input type="checkbox"/>	<input type="checkbox"/>
7. Walking inside, and with an aid if needed	<input type="checkbox"/>	<input type="checkbox"/>
8. Stairs	<input type="checkbox"/>	<input type="checkbox"/>
9. Walking outside (even ground)	<input type="checkbox"/>	<input type="checkbox"/>
10. Walking inside with no aid	<input type="checkbox"/>	<input type="checkbox"/>
11. Picking off the floor	<input type="checkbox"/>	<input type="checkbox"/>
12. Walking outside (uneven ground)	<input type="checkbox"/>	<input type="checkbox"/>
13. Bathing	<input type="checkbox"/>	<input type="checkbox"/>
14. Up and down four steps	<input type="checkbox"/>	<input type="checkbox"/>
15. Running	<input type="checkbox"/>	<input type="checkbox"/>

8.4 PROCEDURE

The data from the DASH outcome measure and FMA measures from subjects in the first phase of the study (125 subjects), as described in detail in Chapter Five and from subjects recruited into the exploratory RCT (37 subjects)(described in Chapter Six) were used for the analysis. Work by Linacre (1994)³⁵⁹ suggests that a sample size of 150 or more will provide 99% confidence of item calibration ± 0.5 logits when performing Rasch analysis. In order therefore to be able to produce best results (taking into account floor and ceiling effects on some of the subjects measures which can be left out of Rasch analysis.) Further data from patients who had been on rehabilitation units in the hospital were also included in the analysis (12 patients). Therefore the data from 174 subjects was used for both the traditional psychometric analysis and Rasch analysis.

8.4.1 ANALYSIS

Analysis of the traditional psychometrics was performed using Statistical software package SPSS version 21. Rasch analysis was conducted using RUMM 2030 software. Dr Afsane Riazi, (Senior Lecturer in Health Psychology, Royal Holloway, University of London) assisted in the analysis of the traditional psychometrics, and checking of the Rasch analysis. Dr Trefor Aspden (Psychology, Royal Holloway, University of London) assisted in the Rasch analysis.

8.5 RESULTS

174 DASH and FMA scores were entered for Rasch analysis. The scores entered were baseline scores for all participants. Due to missing values on two data sets, analysis was performed on 172 subjects.

The mean age of the stroke survivors were 62.6 years (SD 17.7), mean time after stroke was 3 weeks (SD 2.9), 41 % were women. Thirty-five percent of participants had suffered a Middle Cerebral Artery Stroke , with 15% having suffered haemorrhagic bleeds.

8.5.1 DASH ANALYSIS

TRADITIONAL PSYCHOMETRIC ANALYSIS OF THE DASH

The results of traditional analysis mostly supported the DASH as a reliable and valid measure of upper limb function. Data quality was high (no missing data , meaning scale scores were computable for 100% of respondents). Scaling assumptions were satisfied (similar item mean scores, and roughly equivalent corrected item-total correlations). However scale-to-sample acceptability was moderate. Scale scores spanned the scale range and were not notably skewed. However mean scores at 36.0 were not near the scale mid-point, and ceiling effects were high. The internal consistency reliability of the score was found to be high (Cronbach's alpha =0.99) (Table 8.1 details the scores found on the analysis).

Tests of convergent and discriminant validity supported the validity of the DASH. Convergent and discriminant construct validity³⁶⁰ was determined by examining correlations between the DASH and other measures the ABILHAND, FMA, Barthel Index. It was hypothesized that correlations would be highest with the ABILHAND, (another patient reported outcome measure) and then the FMA . Low correlations were predicted for the DASH compared to the Barthel index (as this is a focal measure of functional recovery post stroke, this is described in more detail in Chapter Four). The direction, magnitude and pattern of correlations were consistent with predictions. As forecast, correlations were highest with the ABILHAND (-.85), and then the FMA (-.78). Low correlations were seen for the DASH compared to the Barthel index (-.16).

Table 8.1: Data quality, scaling assumptions, acceptability and reliability of DASH (N=172)

	<i>DASH total</i>
DATA QUALITY	
Item missing data %	0
Computable scale scores %	100
SCALING ASSUMPTIONS	
Item mean scores	1.58 -3.04
Item sd	0.79-1.61
Item total correlation	0.56-0.95
ACCEPTABILITY	
Scale range (possible)	0-100
Score range	0-88.3

	<i>DASH total</i>
Mean score (sd)	36.0 (28.6)
Floor/ceiling, %	0/19.8
Skewness	0.008
RELIABILITY	
Alpha	0.99
Mean inter-item correlations	0.72

RASCH ANALYSIS

Item response-threshold ordering: The threshold between two response options is the location, measured in logits, where the two options are equally likely. Analysis found that three items had disordered response options (two pain questions 24 and 25, and a question regarding ability to write, Question 2), indicating that the proposed scoring function was not working as intended for these items. Respondents seemed to find difficulties in differentiating between moderate and severe response with regards to describing their pain.

Tests of fit. The fit residual test of fit examines the response of each person to each item, and provides evidence that an item might discriminate between different levels of 'symptoms/ disability either more or less than is expected. The fit residual test found that of the 30 items in the questionnaire, 13 had fit residuals outside the recommended range (-2.50 to +2.50). Seven of these items had prominent misfit: 'prepare a meal' (-3.792), 'performing heavy chores (-3.604), 'garden' (-4.111), 'make a bed'(-3.726), recreational activities: little effort' (-4,066), 'sexual activities' (p5.463) less capable' (p 10.053(p5.07)(Table 3) (item location is expressed in Rasch as (p

The chi square test of fit examines, for groups of people with similar total scores (class intervals), the magnitude of departure of the mean score for an item in each class interval from the mean value predicted by the model. This is the most general test of fit and provides a graphical counterpart (the ICC). Chi square probabilities for six items were significant (Table 8.3). Examinations of the graphical indicator of fit (ICC), suggested that the item which under-discriminated the most was writing (question 2). Therefore, patients' responses to items were not consistent with those predicted by the Rasch model.

Differential Item Functioning: No differential item functioning was found in regards to gender or age.

Item locations: This is the location on the Rasch continuum, measured in logits. Ideally, items will have locations that are evenly spaced over a wide range rather than being clustered at the same location. Also, ideally this range of item locations will adequately target the range of locations of the target population. The item locations spread out (from -1.44 to 2.93 logits) indicating that the DASH defined a reasonable continuum (Table 8.3). However examination of the item locations showed that items were not evenly spread along the continuum (Figure 8.2), with a gap at the lower end of the continuum, and two (pain questions 24 and 25) items at the extreme upper end of the continuum removed from the upper reach of person location.

Reliability. Scale reliability was suggested by high Person Separation Indices (0.958). This is comparable to Cronbach's alpha

Local Dependency. Five pairs of items had residuals that were highly correlated (> 0.60), implying that a response to one influences the response to the other. Four of these items appear sequentially in the scale. These pairs of items also had similar content: (questions 7+8, 7+11, 18+19, 24+25, 25+26.) Therefore response bias and dependency is likely to be due to both an overlap of content between items as well as the item ordering.

Tests of unidimensionality: 54 (31.76%) of t-tests of person scores from the item subset comprising the most positively loading items with that comprising the most negatively loading items were significant at the $p < .05$ level. Further, the lower 95% confidence interval corresponded to 28.5% of t-tests significant at the $p = .05$ level. This demonstrated that the assumption of unidimensionality did not hold for this scale. This suggests that the DASH consists of more than one dimension.

8.5.2 THE FUGL- MEYER ASSESSMENT SCORE (UPPER LIMB SECTION) ANALYSIS

TRADITIONAL PSYCHOMETRIC ANALYSES

The results of traditional analysis mostly supported the FMA as a reliable and valid measure of upper limb function. Data quality was high (no missing data , meaning scale scores were computable for 100% of respondents). Scaling assumptions were satisfied (similar item mean scores,). However there was a wide range in item-total correlations (an equivalent correlation demonstrates best scaling). Scale-to-sample acceptability was moderate. Scale scores spanned the scale range and were not notably skewed and mean scores at 69 were near the scale mid-point. However ceiling effects were high, (showing that almost 35% of subjects had near normal ability for all items, and achieving the highest score possible.) The internal consistency reliability of the score was found to be high (Cronbach's alpha (0.99). (Table 8.2 details the scores found on the analysis).

Tests of convergent and discriminant validity supported the validity of the FMA. Convergent and discriminant construct validity³⁶⁰ was determined by examining correlations between the FMA and other measures the ABILHAND, DASH, Barthel Index. It was hypothesized that correlations would be highest with the ABILHAND, (although a patient reported outcome measure, is a measure of upper limb activity) and then the DASH . Low correlations were predicted for the FMA compared to the Barthel index. The direction, magnitude and pattern of correlations were consistent with predictions. As forecast, correlations were highest with the ABILHAND (.78), and then the DASH (.72). Low correlations were seen for the FMA compared to the Barthel index (-.26).

Table 8.2: Data quality, scaling assumptions, acceptability and reliability of FMA (N=172)

	<i>FMA total</i>
DATA QUALITY	
Item missing data %	0
Computable scale scores %	100
SCALING ASSUMPTIONS	
Item mean scores	1.08-1.97
Item sd	0.21-0.84
Item total correlation	0.21-0.95
ACCEPTABILITY	
Scale range (possible)	0-100
Score range	0-94
Mean score (sd)	69(32.6)
Floor/ceiling, %	0/34.9%
Skewness	-1.082
RELIABILITY	
Alpha	0.99
Mean inter-item correlations	0.71

RASCH ANALYSIS

Item response-threshold ordering: The threshold between two response options is the location, measured in logits, where the two options are equally likely. However, response options can be disordered, particularly for items with a higher number of response options, indicating that the extra response options do not provide additional information about a person's true location on the variable that the item represents. For items 1.1.1/1.1.2 thresholds were disordered such that at no point on the ability continuum was option 1 the most probable response option. For a further item 1.6 (another reflex item) whilst thresholds were ordered the response pattern was similar to item 1.1.1/1.1.2 such that response 1 was only the most probable option for a narrow ability range (as seen in diagram 1: Category Probability Curve). This suggests that for these three items a dichotomous response format would be more appropriate.

Tests of fit: The fit residual test of fit examines the response of each person to each item, and provides evidence that an item might discriminate between different levels of 'symptoms/ disability. 8 had fit residuals outside the recommended range (-2.50 to +2.50). four of these items had prominent misfit: Tremor (4.360), wrist flexion/extension-elbow 90° (3.516), volitional movement mixing dynamic flexor and extensor strategies, forearm pronation (3.244), wrist stability-elbow 90° (3.155)(Table 3)

The chi square test of fit examines, for groups of people with similar total scores (class intervals), the magnitude of departure of the mean score for an item in each class interval from the mean value predicted by the model. This is the most general test of fit and provides a graphical counterpart (the ICC).

Chi square probabilities for five items were significant (Table 8.4). Examinations of the graphical indicator of fit (ICC), suggested that the item which under-discriminated the most were the reflex items (1.1.1 and 1.1.2). Therefore, patients' responses to items were not consistent with those predicted by the Rasch model.

Differential Item Functioning (DIF): No items demonstrated DIF by gender or age.

Item locations: This is the location on the Rasch continuum, measured in logits. Ideally, items will have locations that are evenly spaced over a wide range rather than being clustered at the same location Also, ideally this range of item locations will adequately

target the range of locations of the target population. The Item locations were spread over a wide range (-4.473 to 3.071) (Shown in Table 8.4) and targeted the range of person abilities with the exception of a number of individuals who demonstrated no impairment (who demonstrated full ability).

Reliability. Scale reliability was suggested by high Person Separation Indices (0.96). This is comparable to Cronbach's alpha

Local Dependency: The ability on one type of hand grasp was seen to be highly correlated with the ability on other types of hand grasp. This was also seen in the wrist items. There was dependency amongst different shoulder items such that performing some shoulder movements were dependent on being able to perform other shoulder movements. As these shoulder movements may represent different points along the recovery/ability continuum it may be preferable not to delete dependent items. Instead a testlet could be formed out of shoulder items, to provide an item representing the range of shoulder movement ability.

Tests of unidimensionality: 18 (10.59%) of t-tests of person scores from the item subset comprising the most positively loading items with that comprising the most negatively loading items were significant at the $p < .05$ level. Further, the lower 95% confidence interval corresponded to 7.3% of t-tests significant at the $p = .05$ level. This demonstrated that the assumption of unidimensionality did not hold for this scale. This suggests that the FMA score consists of more than one dimension.

8.6 DISCUSSION

The aim of this chapter was to look at the measurement properties of the upper limb scales used in the study. In particular this was performed in detail for two of the measurements used- DASH a patient reported outcome measure and a clinician reported measure –the FMA upper limb scale.

This detailed analysis was performed in line with the MRC framework, and in keeping with FDA²⁴⁸ and EMEA guidelines³⁴⁹. These guidelines discuss that to formally evaluate an intervention it is essential that the outcome measures used capture the benefits of that

intervention. Furthermore, rigours testing of scales allows identification of which outcome is most sensitive to change.

This discussion will now focus on the results from the analysis of the two measures separately.

8.6.1 DASH

Traditional psychometric evaluation mostly suggested that the DASH was a robust measure, although marked ceiling effects were found. Rasch analysis found a number of problems with the scoring and items in the DASH. Each of these analyses will now be discussed separately:

More than the recommended 20% ³⁵³ of participants (34.9%) were found to rate that their upper limb did not cause them marked difficulties with use of the DASH score on traditional psychometric analysis. Previous literature³⁶¹ looking at the scaling qualities of the DASH as an upper limb outcome score in the Multiple Sclerosis population did not find this marked ceiling effect (Cano et al (2011)³⁶¹ found no problems with the DASH score when using traditional psychometric analysis.) It is difficult to evaluate why these different results were found. This may be due to the different sample populations used in the two analyses (the analysis described in this chapter and the analysis described in Cano et al (2011)³⁶¹, which analysis the DASH in people with MS). As far as the author of this thesis is aware, the DASH has not been previously evaluated in a stroke population. Further analysis of this measure in stroke is therefore required to see whether the high ceiling effects noted in this current analysis is sample specific

A high ceiling effect was also found when performing psychometric analysis on the measures from the results of the recruitment study, detailed in Chapter 5. A possible explanation for the problems seen in targeting of the measure was the high proportion of participants recruited into the first part of the study that had no upper limb deficit. This also raises the need to perform further analysis of the DASH in acute/subacute people with stroke to reveal whether this effect is seen in other samples.

Rasch analysis of the DASH also illustrated some other problems with the measure. These will now be discussed. Rasch analysis showed that several items (pain questions 24 and

25 and writing question 2) had a high amount of variance not explained by the rest of the scale and that several items were redundant, in that a very high proportion of their variance was explained by the rest of the items in the scale. This means that these questions could be left out of the score.

Previous studies using the DASH in a sample of people with MS found that four categories may have worked better than five²⁵⁹. In contrast to this previous work³⁶¹ the five response options worked well in this study for most questions. The exception to this was seen in regard to the pain questions where floor effects were observed with the majority of respondents choosing the first two response categories (no or mild pain). These floor effects in the pain items may be specific to the population of respondents in the present study, all of whom were very recently post stroke (mostly six weeks after stroke). It would therefore be important to repeat these analyses in this patient group and other stroke groups to determine whether the findings of this study are generalisable.

A high number of items were found to 'misfit' (13). This has also been seen in previous literature³⁶¹, which found similar misfit. The fit problems may be a reflection of the scale contents. This is because from a clinical perspective, the DASH items cover a wide range of constructs; some items measuring symptoms, others physical function, and others psychological well-being.³⁶¹ Cano et al (2011)³⁶¹ argue that although these items are clinically relevant, they form conceptually disparate elements, therefore summing these together into a 'symptom disability score' is inappropriate. This has led Cano et al³⁶¹ to suggest that the DASH is capturing a wider construct than just upper limb functioning. Analysis of the unidimensionality of the scale also suggested this, as analysis found the scale not to be unidimensional.

Few participation measures are available in stroke research²⁵⁴, and this is particularly so when looking at use of the upper limb post stroke²¹⁴. However, there is a growing call to use these measures in stroke research. The DASH was originally developed using traditional psychometric methods for people with musculoskeletal disorders. It is therefore unsurprising that there are problems translating this measure to a stroke population. However, this analysis has shown that traditional psychometric evaluation implied good validity and reliability in the measure, although found a high ceiling effect. Rasch analysis unmasked further limitations in the scale with disordered response categories, and item misfit. However, to allow the findings of this study to be generalisable to the acute stroke

population, it would be important to repeat the psychometric analysis, in a larger size population with upper limb difficulties.

8.6.2 FMA UPPER LIMB SECTION

Similar findings to that of the DASH were seen when performing psychometric evaluation of the FMA upper limb section. Just as in the DASH evaluation, traditional psychometric evaluation found marked ceiling effects with the measure. The scale has been considered in the literature as a 'gold standard' measure^{275,276,362}, and considerable tradition psychometric evaluations have been performed looking at its measurement properties^{275,276} which have been found to be excellent. Some work has commented on ceiling effects with the measure in people who have mild stroke³⁶² (This was substantiated in this analysis.)

Rasch analysis also found a number of problems with the scoring and items in the FMA. This is consistent with previous literature which has examined the psychometric properties of the FMA using Rasch analysis²⁸⁰.

The pattern of response thresholds for the three reflex items indicates that people are responding to these items in a dichotomous manner. Therefore, a dichotomous response format would be more appropriate. The reflex items, particularly the flexor and extensor reflex items, were discriminated between patients, with patients of all ability levels tending to score the maximum on the flexor and extensor items. Thus these items do not contribute to the scales ability to differentiate between people of different ability levels in patients who have had acute stroke. This has also been seen in previous work which has evaluated the FMA using Rasch analysis²⁸⁰. Woodbury et al²⁸⁰ removed the reflex items from the scale to improve the scales validity.

Ability to perform one type of hand grasp was seen to be highly correlated with the ability to perform other types of hand grasp. This was also seen in the wrist items. A dependency amongst different shoulder items was also seen (in the flexion synergy section of the score), such that performing some shoulder movements were dependent on being able to perform other shoulder movements. Hsieh et al³⁶³ removed some wrist, hand and shoulder items when making a shorter Fugl Meyer score following Rasch analysis.

However as these movements may represent different points along the recovery/ability continuum it may be preferable not to delete dependent items. Instead a testlet could be formed out of the wrist, grasp and shoulder items, to provide an item representing the range of arm movement ability.

Woodbury et al²⁸⁰ looked at the item arrangement and ordering of the FMA. They discuss that the measure was initially devised with the intention of measuring upper limb recovery. Items were therefore ordered from easy to hard to map this process. As part of Woodbury et al²⁸⁰ assessment of the validity of the FMA they looked at the difficulty ordering of items and found Rasch generated item difficulty ordering to be different from than that proposed by Fugl- Meyer. This was not looked at in detail in this current study, as the aim of this work was to compare traditional and newer psychometric methods in regard to the FMA. However the dependency in some items as described above may point to similar findings with the ordering and items in the measure. Both this dependency and ordering issues in the measure may also explain why testing of the unidimensionality of the measure found that it was not unidimensional.

8.7 CONCLUSION

The evaluation of novel interventions (such as the use of a robotic arm in upper limb rehabilitation post stroke) increasingly depends on the use of valid, reliable and responsive outcome measures³⁰⁶. Psychometric analysis of scales plays a key role in scale development and testing, to ensure that scales provide scientifically robust, clinically meaningful, and clinically interpretable results²⁴⁵. This study has highlighted the importance of using both 'newer' psychometric analysis methods such as Rasch analysis, along with traditional psychometric analysis to uncover limitations and problems with a scale. This current analysis provided an initial evidence base to improve/ change the DASH and FMA upper limb score for use as a research tool in acute stroke research.

Marked ceiling effects were found with both of the measures. This corresponds to the work discussed in Chapter Five where similar ceiling and floor effects were found with the measures in the first phase of the study. This could be a reflection of the complex nature of upper limb recovery following stroke. Some patients, with relatively mild injury, have potential to recover useful function such as the ability to use the hand to hold and

manipulate objects, others with more severe injury may not be able to use their arm for tasks such as that but may use it to stabilise an object (such as rest hand on a page of a book to allow unaffected hand to turn the page). This complexity makes it hard for a scale to reflecting clinical important change in clinical and research practice in arm function. The analysis performed in this chapter elucidated limitations in measures that have been used as “gold standard” upper limb scales ³⁶². However there is a lack of a validated measure suitable ^{214, 306} Chen and Winstein (2009)⁹⁷ echo this view suggesting that there is an urgent need to develop such measures. The work performed in this thesis concurs with these views. Further discussion on this will be made in the next and final chapter.

Table 8.3. Dash Item fit statistics ordered by chi-square probability

Item	Item label	Location	SE	Fit Statistics	
				Residual	Chi-Square
I0001	Open a new jar	-0.572	0.125	-2.832*	10.7
I0002	Write	0.817	0.102	2.966*	69.962*
I0003	Turn a key	0.266	0.114	1.816	5.356
I0004	Prepare a meal	-0.643	0.13	-3.792*	9.697
I0005	Push open a heavy door	-0.138	0.125	-1.62	6.091
I0006	Place an object on a shelf	-0.247	0.123	-3.104*	7.281
I0007	Do heavy chores	-0.91	0.122	-3.604*	4.906
I0008	Garden	-1.004	0.122	-4.111*	4.358
I0009	Make a bed	-0.617	0.122	-3.726*	7.841
I0010	Carry a shopping bag	-0.684	0.122	-1.676	2.983
I0011	Carry a heavy load	-0.858	0.124	-2.865*	2.843
I0012	Change a light bulb	-0.948	0.124	-3.258*	4.318
I0013	Wash your hair	-0.143	0.123	-3.097*	13.369*
I0014	Wash your back	-0.227	0.124	-1.727	4.869
I0015	Put on a pullover	0.295	0.124	-2.094	7.337

Item	Item label	Location	SE	Fit Statistics	
				Residual	Chi-Square
I0016	Use a knife	0.046	0.123	-1.559	5.79
I0017	Recreational activities: little effort	-0.368	0.125	-4.066*	12.897
I0018	Recreational activities: force or impact	-1.394	0.122	-2.113	0.429
I0019	Recreational activities: move arm freely	-1.439	0.122	-1.776	0.325
I0020	Transportation needs	-0.253	0.11	-0.575	5.505
I0021	Sexual activities	0.273	0.106	5.463*	12.272
I0022	Interference with social activities	-0.21	0.11	0.833	1.133
I0023	Limited in work	-0.411	0.121	-1.599	1.407
I0024	Pain in arm, shoulder or hand	2.93	0.138	0.87	16.213*
I0025	Pain performing an activity	2.881	0.137	0.934	17.548*
26	Tingling in arm, shoulder or hand	1.296	0.123	1.654	38.637*
I0027	Weakness in arm, shoulder or hand	0.103	0.121	-1.11	4.154
I0028	Stiffness in arm, shoulder or hand	1.182	0.119	1.092	6.452
I0029	Difficulty sleeping	1.588	0.128	1.626	5.72

Fit Statistics					
Item	Item label	Location	SE	Residual	Chi-Square
I0030	Feeling less capable	-0.614	0.125	10.053*	58.348*
*indicate items falling outside of recommended limits					

Figure 8.2: Graph showing item location for the DASH

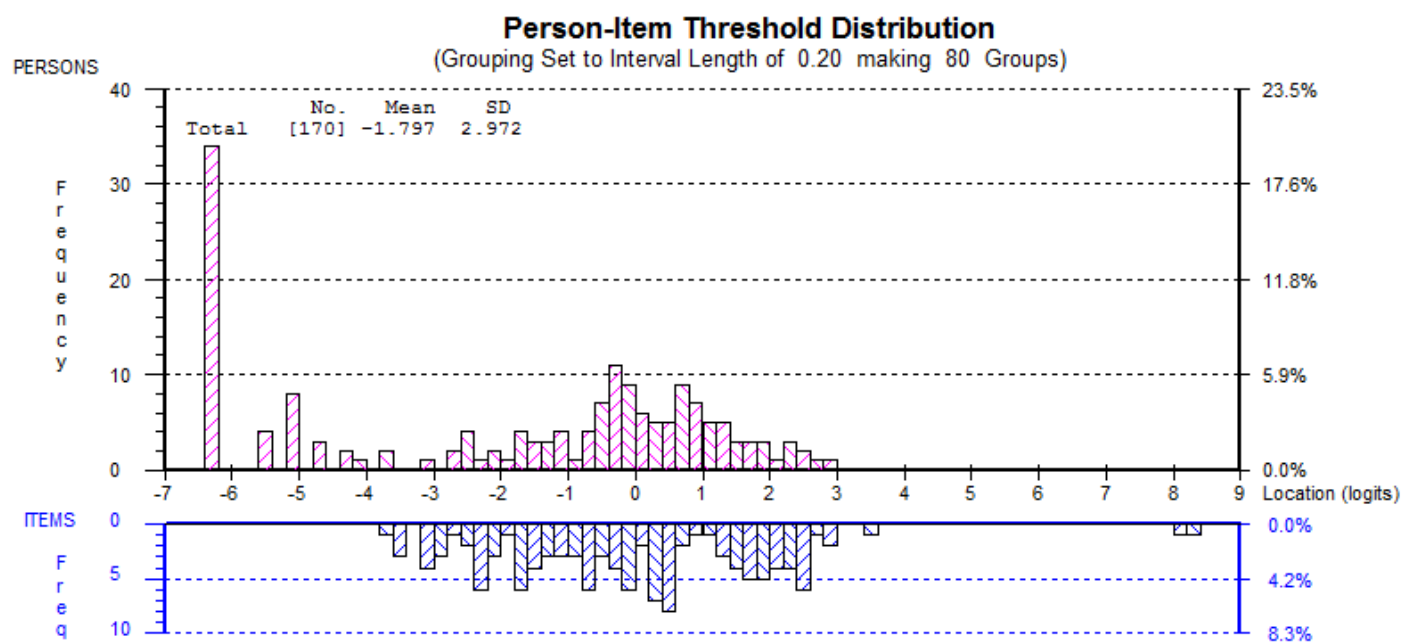


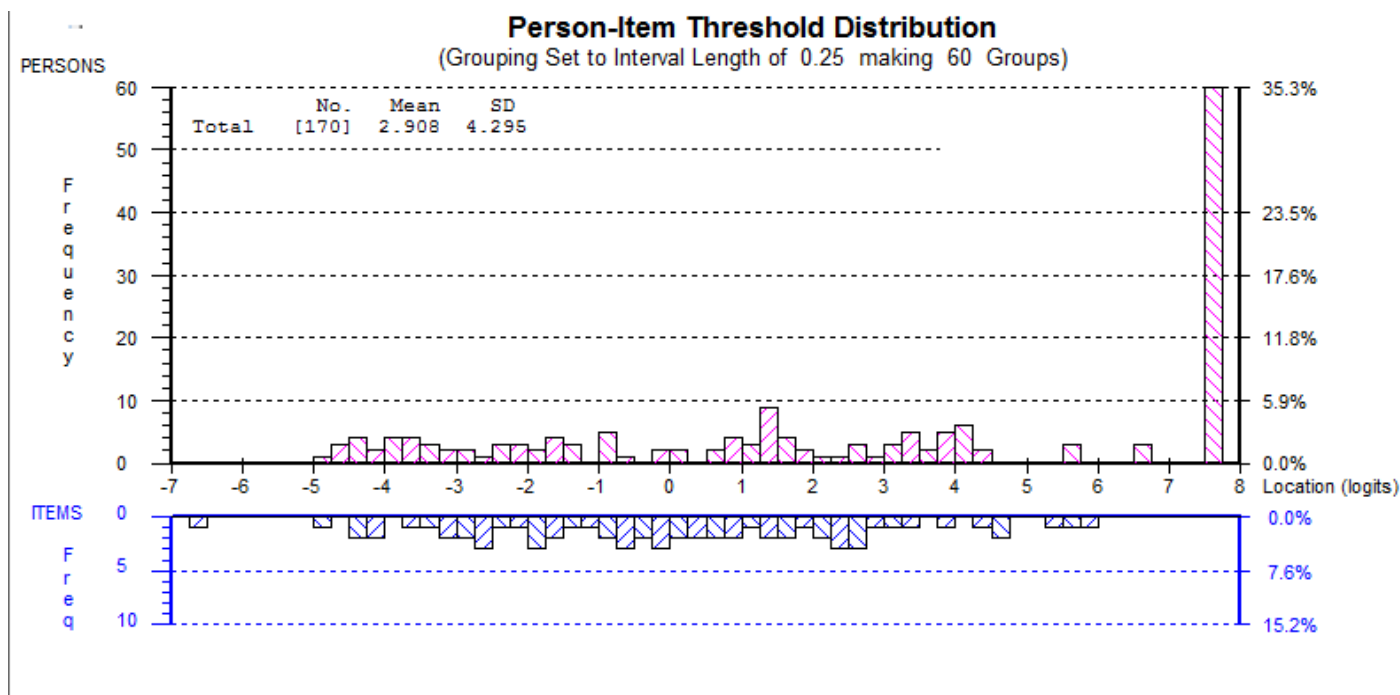
Table 8.4: FMA Item fit statistics ordered by chi-square probability

				Fit Statistics	
Item	Item label	Location	SE	Residual	Chi-Square
1.1.1		-4.473	0.256	0.035	19.518*
1.1.2		-4.301	0.25	0.229	29.158*
1.2.1		-3.54	0.298	0.462	1.499
1.2.2		-1.827	0.234	0	0.134
1.2.3		-1.332	0.229	-0.375	0.507
1.2.4		-0.732	0.224	0.219	0.482
1.2.5		-1.258	0.234	-0.395	4.925
1.2.6		0.021	0.225	-2.503	6.304
1.3.1		-0.953	0.226	-1.507	5.161
1.3.2		-0.328	0.223	-2.888	8.604
1.3.3		-0.131	0.223	-1.883	6.088
1.4.1		-0.18	0.226	-0.461	0.15
1.4.2		-0.487	0.224	-1.9	5.159
1.4.3		0.393	0.224	-3.244	8.509
1.5.1		-1.287	0.228	-1.447	3.598

				Fit Statistics	
Item	Item label	Location	SE	Residual	Chi-Square
1.5.2		-0.529	0.223	-0.905	1.942
1.5.3		0.2	0.224	-2.787	5.177
1.6		-2.912	0.229	0.625	48.462*
2.1		0.297	0.223	-2.288	2.813
2.2		0.659	0.225	-3.516	7.591
2.3		0.969	0.225	-3.155	5.854
2.4		0.905	0.224	-2.919	5.164
2.5		1.239	0.224	-0.384	0.342
3.1		0.629	0.227	-0.765	1.819
3.2		1.184	0.229	-1.813	3.03
3.3		2.718	0.263	-0.375	0.182
3.4		3.071	0.264	-1.167	3.799
3.5		2.516	0.24	-0.746	5.96
3.6		2.442	0.242	-1.147	4.168
3.7		2.296	0.237	-1.118	3.178
4.1		0.584	0.223	4.26	37.322*

				Fit Statistics	
Item	Item label	Location	SE	Residual	Chi-Square
4.2		1.589	0.234	0.408	21.701*
4.3		2.555	0.258	-0.541	8.245
*indicate items falling outside of recommended limits					

Figure 8.3 Graph Showing Item locations for the FMA.



CHAPTER 9: FINAL DISCUSSION

9.1 INTRODUCTION

This chapter will draw together the interrelated strands of this thesis, providing summary and discussion. Initially a synopsis of each chapter will be given and then the main aims and findings will be explored with discussion of limitations and strengths. Finally future work that has been identified through the studies will also be explored.

9.2 BACKGROUND AND SUMMARY OF FINDINGS

Stroke is currently the single largest cause of adult disability in the United Kingdom with one third of people who have had a stroke left with long-term disability. Arm recovery post stroke is particularly poor.

This thesis was concerned primarily with recovery of arm movement following stroke. The main aim was to investigate the feasibility and practicality of the use of a novel adjunct to arm rehabilitation (use of ReachMAN robotic device) in the clinical setting, building on the available literature to explore the translation of robotics from experimental research into use in clinical practice. This overriding aim also encompassed 1) investigating who would benefit from use of the device, 2) investigating whether the novel intervention itself was of benefit to assist arm recovery post stroke 3) Evaluation of upper limb outcome measures in order to truly assess the value of the novel intervention.

First, **Chapter One** gave a general background on stroke, and the impact a stroke can have functionally, cognitively and psychologically. In particular the paucity of upper limb recovery was described. The use of increased intensity, with increased repetitions of movements was discussed as a way of improving arm movement and recovery. The use of rehabilitation robotics emerged as a means to achieve these aims.

Chapter Two, then presented a literature review of the evidence behind the use of robotic devices as an adjunct to arm recovery. This review highlighted unanswered questions regarding the use of this invention, in particularly the translation of rehabilitation robotics from research to clinical practice: **Chapter Three** reiterated the unanswered questions that the thesis hoped to address which were to: clearly define the best outcome scales to use, evaluate who could potentially use the device, then test the efficacy of the intervention within a defined population using appropriate outcome measures and a mixed methodological approach, finally perform psychometric analysis using new & traditional methods to evaluate and select the most appropriate outcome measures for future trials.

Chapter Four described a systematic literature review to establish the most reliable, valid and responsive available limb outcome scales to use in the trials described in the thesis. This found that three measures best met the psychometric criteria: Chedoke Arm and Hand Inventory, Stroke Rehabilitation Assessment of Movement upper limb section, and ABILHAND. However additional measures were also included to ensure the results were understood by the wider research community and were reproducible. The battery of measures chosen incorporated a mixture of clinical rated and patient reported outcome measures: These were the: STREAM, CAHAI, ABILHAND, FMA, ARAT, EQ5D, SF36, Barthel Index, NIHSS and DASH.

Chapter Five described an evaluation of consecutive acute stroke patients to establish the proportion of acute stroke patients that could potentially benefit from rehabilitation using ReachMAN. This found that people with severe arm impairments could use the device. Participants needed to be able to sit out for at least ten minutes, if not longer to be able to interact with the device, and be able to attend to the task for this time with adequate vision to see the screen. 125 people who were within a week of having a stroke were recruited to

this phase of the study. 45% of these participants presented with some degree of upper limb deficit, of which 46% were able to interface with a mock up of the ReachMAN device (pReachMAN). There were some problems found with the targeting and acceptability of the battery of outcome measurement scales (this will be further discussed later in this chapter)

Chapter Six described a preliminary randomised control trial aiming to determine how the use of a robotic device (ReachMAN) could be delivered in practice. This found that the use of ReachMAN was practical and feasible in a sub acute stroke population in participants who were inpatients in rehabilitation units. This study did not completely disprove the null hypothesis that the use of a ReachMAN makes no significant difference to the recovery of the arm after stroke. This was because from the battery of outcome measures only one measure the ABILHAND found a statistical significant change between the control group and the intervention group .A trend for improved arm movements was seen in the intervention group with the other measures. This was particularly seen with the FMA upper limb score where an almost doubling of the Standard deviation (when compared to the control group) of change scores between baseline and six weeks. Correlations were found on subgroup analysis of FMA scores in the control group with level of arm impairments (severely armed impairment correlated with lower change in FMA scores on six week measurement). However this was not found in the robotic (intervention) group, this suggested that level of impairment did not influence any potential benefit from the device.

Qualitative interviews with participants who used ReachMAN provided rich data on perceptions of the robotic device (Described in **Chapter Seven**). Participants generally described the intervention, when it did not cause pain, as having a positive impact on function and movement in their arms. They found it motivating and enjoyable. However

they also found it tiring. This fatigue was also noted in the RCT, where 20 minutes use of the robot was the average length of time it was used for. This is a shorter period than previous literature, but had been reported in one other study on early stroke participants. Doornebosch et al (2007) ²²⁶ found sub-acute stroke patients were able to use a robotic device for on average 20 minutes a day (when fatigue prevented them using the device for longer periods).

Chapter Eight described detailed psychometric analysis of the two of the outcome measures used: DASH and FMA. This was performed to rigorously test the measures to ensure targeting and acceptability in order to truly assess the value of the novel intervention. This analysis found problems with both measures. In particular ceiling effects were seen with both, suggesting that in any future studies any participants with mildly impaired arms, if included in the study, may need other measures to assess their change with the intervention. The analysis also suggested means to improve the measures for future use (such as removing the reflex questions from the FMA).

In summary the main messages identified from this thesis are:

- 1) The use of a robotic device was found to be a feasible and practical intervention for subacute strokes who were undergoing inpatient rehabilitation.
- 2) The device was able to be used by a wide range of arm impairments, including people with severely impaired arms. The level of severity of arm impairment did not seem to impact on any benefits in arm function seen with use of the device.
- 3) Although significance was found with only one of the measures, trends were also seen to suggest benefit from use of the robotic device and this was strongly reported by participants.

- 4) Problems were seen with the targeting and acceptability of the battery of outcome measures suggesting a need to develop an upper limb measure that addresses the shortfalls found.

9.3 LIMITATIONS

The studies were designed in accordance with the MRC framework for the development of complex interventions and in correspondence with this guidance ²³⁸ a multi-layered approach was used, combining a number of different studies and methodological approaches.

However, there were weaknesses in the studies and these will now be discussed:

9.3.1 GENERAL LIMITATION WITH THE METHODOLOGY USED IN THE STUDIES

The studies were carried out in a single center in central London which provided specialised stroke care. This limits the abilities to generalise the results found to the wider stroke population, for a number of reasons: Participants were recruited from a Level One (complex specialised rehabilitation in a tertiary referral) rehabilitation unit in the RCT study, which tends to take younger patients who need a longer period of rehabilitation than that usually afforded in stroke rehabilitation services; both of these factors could have influenced the results as well as the generalisability of the study.

The studies were exploratory in nature, with low population numbers in all stages of the study which also makes it difficult to generalise results to the wider stroke population. Work by Lincare (1994)³⁵⁹ suggests a sample of 150 is required for accurate psychometric evaluation (data was collected in Phase One on 125 participants only). The pilot RCT did not recruit to its ideal number of a total of 40 participants, and power calculation from the

results of this study suggests that 146 subjects are required to fully test the hypothesis (using the assumption of 5% significance and 80% power).

The effects of a therapeutic intervention for the stroke population may vary, depending on the phase of recovery of the individuals included in the study. More rapid recovery can be expected within the first six months after stroke, and, this may be due to natural recovery. The extent to which natural recovery is facilitated or obstructed by external factors is not known. In the chronic phase, where recovery may have slowed or plateaued, it may be easier to evaluate the effects of an intervention. The effect of natural recovery may well have influenced the results seen in these studies. However, natural recovery would have influenced the results of both the control and intervention group in the exploratory RCT. The prevailing aim of the studies was to bridge the link between research and clinical practice, more patients are seen clinically in the subacute phase when potential for recovery is greater¹⁰⁹. Furthermore, fewer studies have looked at robotics in the subacute phase post stroke, and this gap in the literature was another focus for the thesis.

The people recruited to the studies represented a heterogeneous population, including those with both haemorrhagic strokes and infarcts. Although this mirrors the population treated in clinical practice, the research design could be criticized for including people with haemorrhage as this type of stroke has a different aetiology and, sometimes prognosis, from infarcts that comprise the majority of strokes. The participants with haemorrhage were evenly distributed across both groups in the RCT and so it is unlikely that the results were affected by the different diagnoses. If people with haemorrhagic stroke are to be included in future studies it may be that the groups should be stratified by stroke classification.

Furthermore, a broad upper limb impairment inclusion criteria was used in the RCT, this again was a heterogeneous population and no stratification for arm function was used. Future trials would benefit from subjects being stratified according to severity of arm impairment (such as stratification according to FMA UL scores at baseline: A FMA scores: 0-15 representing severe impairment, moderate impairment 15-38, mild impairment 38-66²⁷²). The recruitment study (phase 1) found that subjects with mild upper limb deficits found using the robot too easy. Due to the marked ceiling effects seen with the measures, in conjunction with this finding in the recruitment phase, suggests that subjects with mild upper limb deficits could perhaps be excluded from future trials.

In practical terms this would have meant excluding three subjects from the RCT (two in the control group and one in the intervention group) who had baseline FMA scores of above 38. Subgroup analysis (as reported in Chapter Six) found no significant change if these subjects were excluded from the analysis.

Research trials often have difficulty in recruiting to target and both trials experienced some problems in recruitment. The recruitment study took a year to complete (longer than had been anticipated). It had also been hoped that the RCT trial would be completed by the end of January 2011. In fact, although recruitment continued until the end of March 2011, it was not possible to reach the target of 40 participants. Factors that may have affected recruitment to both phases included the increased use of thrombolysis, and the reduced length of stay within the hyper acute stroke unit and ABIU. Data on the use of thrombolysis and length of stay are not available in entirety over the time frame of the studies and so it is not possible to confirm whether or not these factors influenced recruitment. Although recruitment was higher than used in other research studies^{324;140} the low recruitment rate limits the generalisability of the results as only a small proportion of

the eligible population took part and may not therefore have been representative of the population as a whole.

9.3 2 SPECIFIC LIMITATIONS WITH THE STUDIES.

Each chapter has detailed limitations within the studies. A further critique of some specific issues from the studies will now be explored.

With reference to the RCT described in Chapter Six, the trial was not blinded. Wade et al (2006)³²³ have commented on the difficulties of performing double blind RCT to evaluate rehabilitation. It is difficult to blind either the participants or the therapists in studies of a novel treatment adjunct. Some clinical trials of robotics have the control group performing sham tasks on the robot^{199;364;173} but this could be argued involves additional upper limb movement, so could impact on the results. However an independent assessor who is blinded to the group allocation could have performed the outcome measurements. This should be included in any future trials looking at the ReachMan device.

A further limitation of the RCT is that it could be argued that any improvements seen in the intervention group was due to the additional input the group received (time spent on the robot in addition to their usual therapy) and that any additional arm therapy, regardless of the content of this therapy may lead to improved arm function. Any future studies looking at the intervention would benefit therefore from adding matched additional arm therapy in the control group to the time intervention group spends on the robot. (A third “active control” group).

Recent clinical trials looking at robotic intervention have used this strategy. Masiero et al (2011)²⁰² performed a clinical trial on 21 subacute stroke subjects. This study compared conventional therapy (40 minutes of treatment to the proximal arm in addition to patients

normal inpatient therapy), with use of the NeReBot robotic device for two 20 minute training session (these patients also received their usual inpatient therapy). Interestingly this study found improvements in arm movements in both groups but no difference between the groups. This suggests that additional therapy in whatever form assist with improving arm recovery. A study by Burger et al (2011)¹⁹⁹ also found similar results when matching the intensity of conventional therapy to robotic therapy. In contrast, Liao et al (2011)¹⁸⁶ investigated the use of Bi-Manu –tract in ten participants in chronic stroke subjects, and compared dose-matched control and intervention groups. This study found a statistically significant improvement in the FMA measure with use of the robot in comparison to the control group. The disparity of results between studies adds further weight for the need for further clinical trials to investigate dose-matched control and robotic therapy.

Records of the conventional therapy provided to the participants were not available in all cases. It was not therefore possible to evaluate how much time was spent on the upper limb in the control group. There is no easy way to resolve the problem of ensuring the completion and return of conventional treatment records. Although the information required from the therapists was kept as brief as possible (a single sided sheet, mainly completed by ticking boxes), Therapists reported this was not completed if they felt they had other duties which were more pressing. Furthermore, due to the length of time the trial ran for, there was a considerable change in staffing of therapists (due to rotations, and staff leaving), requiring regular training of staff. Similar findings were found in a RCT of an upper limb treatment intervention¹⁶¹ where again insufficient completed record of conventional therapy made analysis of this not viable.

Unpacking the black box of what conventional therapy comprising of, and how much time is spent on upper limb activities as part of routine therapy remains an important area³²³. One way of addressing this is to try and make the completion of conventional records a part of routine clinical practice therefore it is already established before a clinical trial is commenced. This may be possible in a single site centre (and is being initiated at NHNN), but may prove to be harder over a multi site trial.

9.3.3 LIMITATIONS WITH THE REACHMAN DEVICE ITSELF

The novel robotic device used in the studies discussed in this thesis was designed uniquely for the trials themselves. The device was designed in collaboration with clinicians (Research Therapist Karen Baker, Consultant Physiotherapist Ann Holland, and Consultant Neurologist Diane Playford) and engineers (at Imperial College). This allowed the machine to be designed with specific recommendations in mind (to be low cost, simple to use, place arm in good alignment) however this also meant it was very much in the preliminary stage of design.

In practice this presented with a number of issues: the machine broke down on numerous occasions during the trial, and this impacted on the number of sessions the participants were able to use it for. The hand and wrist component of the machine (which allowed hand opening and closing) was extremely sensitive and regular adjustments were needed to this component of the device. The device was not able to be used independently by participants (this will be explored later in Section 9.4.3), was not portable in nature in its current design and was found not to be challenging for people with mild arm impairments.

Chapter Seven described participants ideas on areas that needed changing with the device, and these areas would need to be addressed and an updated model of the machine required prior to future use

9.4 FACTORS AFFECTING THE TRANSLATION OF ROBOTICS INTO CLINICAL PRACTICE.

Chapter Two outlined the unresolved issues and questions impacting on the translation of robotics from research into clinical practice. This thesis attempted to address some of these areas and these will now be discussed.

9.4.1 INTENSITY OF PRACTICE

Research on upper limb recovery, suggests that increased intensity of therapy and repetition of practice are seen as the best means to maximise recovery of arm movement and function.¹⁶⁴ Up to 300-500 repetition of a movement has been recommended to enhance motor learning³²¹. It has already been previously discussed that it is unknown the amount of movement and repetition the subjects in the control group of the RCT were receiving. In the intervention group, subjects were found to move their arm 150-200 reps and for a maximum of 20 minutes five days a week. This is lower than the additional practice the literature³²¹ suggests is beneficial for improvements in arm movement. This may therefore be indicative for the lack of statistically significant differences between the groups (although statistical significant change was found with the ABILHAND). However trends toward improvement in almost all outcome measures were seen in the robotic group compared to the control group. This points to a suggestion that even a small increase in the time and repetition of arm movements can make a difference to arm function in sub acute stroke patients.

The interviews highlighted that participants in the intervention group reported they were unable to spend more than this time using the robot. However some expressed they would have liked to use the robot more than once a day. This could be a means to increase the intensity of using the device, for example its use for two 20 minutes sessions a

day. The practicality of achieving this in a rehabilitation environment may however prove to be difficult. The loss of robotic sessions described in Chapter 6, Table 6.3 illustrated the busy nature of subjects day when in the rehabilitation units, adding extra session to this may prove challenging.

9.4.2 PATIENTS PERCEPTIONS OF THE DEVICES

Interviews with participants who used the robot (included in Chapter Seven) described that they reported that they enjoyed using the robot and found it motivating. They also expressed enjoyment in participating in a research project and the fact that the study involved using a novel device added to their enthusiasm. The same enthusiasm may not be shown if using a robotic device is introduced as a standard therapeutic adjunct, which may adversely affect motivation to use it. Therefore, it is possible that an element of the Hawthorne effect occurred, where the participants are merely reporting more benefit due to being involved in the study. Theories of learning suggest that the perceived relevance of an activity to an individual has an effect on learning ²¹⁸. If the person considers that the treatment may lead to an improvement in the hand and arm then they may be more motivated to attend during the treatment sessions. This may have been an element to consider in the intervention group and also if the device was to be used in routine clinical practice.

9.4.3 INDEPENDENT USE OF THE ROBOT

Another view that was raised from the interviews was that participants expressed a strong desire to independently use the robotic device. Participants were unable to switch on the programme independently to use the machine. The main physical barrier to independent use was the inability to place the paretic arm into the robot arm support independently.

Previous studies have also reported difficulty with independent arm attachment ^{224;134;226}. The ACRE 2 device ²²⁶ utilised a touch-screen computer interface to facilitate the patients to initiate and control the device during a session. This could be considered for the next model of the ReachMAN device.

The ultimate goal of rehabilitation robotics is to facilitate supplementary independent practice ²¹⁰. However independent use of the device (or with help from a relative/carer) would itself raise a number of issues:

- Is there something special about the patient-therapist relationship that enhances the intervention?
- Does the therapist have skills that allow them to progress the treatment, and respond to changes in the presentation of the patient, that an un-qualified person would lack? If so, could this be adequately addressed by regular reviews with a trained therapist?
- Would there be a benefit in using a robotic device on a daily basis (rather than weekdays only)?
- Would patients with self- directed practice actually use the device daily?
- Is too much expected of carers already, and would they feel obliged to provide the treatment if they were asked to?

The RCT found that rehabilitation assistants were able to guide the participants with using the device, and weekly reviews by a trained therapist were sufficient. How this could be achieved with people with arm impairments using the device independently needs further thought.

The interview with carers did not throw any information as to whether they would be happy to assist their relative with independent use of the robot. As this was not a reality

during the study, this may have explained why carers did not mention this when being interviewed. This information may only come to light when this does become an applicable option.

9.4.5 RISKS WITH THE DEVICES

Chapter Two discussed that current robotics literature suggests that dropout rates from clinical trials using robotic devices were very low and adverse reactions were rare²⁰⁵. This was also seen in the RCT where only one person dropped out of the study due to shoulder pain. Chapter Six and Seven explored in further detail this subject's wish to cease the intervention and his shoulder pain, and although the MDT felt use of the robot did not hugely impact on his pain, he himself felt this was the case. It is difficult from this single incident to infer risk with the use of the device. However this did demonstrate the importance of systematic reporting of adverse events and stressed the importance of the continuation of this with any future trials.

9.4.6 WHAT PROPORTION OF ACUTE STROKE PATIENTS COULD POTENTIALLY BENEFIT FROM USING A ROBOTIC AID?

The first phase of the study aimed to address the question of how many people could potentially benefit from using a robotic aid. This found that almost half of people who had a stroke and who had arm impairment were able to interface with the robotic device, and could potentially benefit from its use.

This is of important clinical significance as it illustrates that a large stroke population (wide range of arm impairments) can potentially benefit from the intervention. This is in contrast to constraint-induced movement therapy which has been found to have the most robust evidence supporting its use³⁶⁵. A major challenge with constraint-induced movement therapy is that trials focus on selective populations (in particular those with some

preservation of wrist and finger extension) who are able to tolerate long periods of constraint.

9.4.7 WHAT SEVERITY OF ARM IMPAIRMENT CAN USE THE DEVICE AND IS THERE A DIFFERENCE IN THE POTENTIAL BENEFIT OF THE AID DEPENDING ON THE SEVERITY OF ARM PARESIS?

A wide range of impairment levels were found to be able to use the robotic device, and this led to a wide range of differing arm impairments levels in the RCT.

Sub analysis of the FMA scores looking at any potential difference depending on severity of arm impairment seemed to suggest that participants with severely impaired arms benefited as much from using the device as did people with more movement in their arms (while this did not seem to be the case in the control group where more arm movement at baseline correlated with better improvement in movement following six weeks of conventional therapy).

Severe arm impairment is prognostic of poor recovery⁹². At present there is little therapy specifically to promote recovery of the severely paretic or paralysed upper limb after stroke. In patients with severe upper limb paresis. This may be because the ability to participate in repetitive task –orientated activities is limited because they have insufficient underlying movement¹⁵⁴. This may explain why stroke patients with severe paresis show limited improvement¹⁵⁴. Robotic devices may be a means for these patients to perform repetitive, task-specific activity. The RCT suggested that the use of the device may be beneficial for those with severe arm paresis. .

Other trials^{161;366} looking at different treatment modalities to assist with upper limb recovery have also found that although, the group as a whole may struggle to achieve significant change, some stroke survivors respond more than others to the same intervention. Rather

than the “one size fits all” treatment that is currently used in research, it may be possible to determine which individuals will respond to which treatment by looking for predictors of response in their baseline physiology or impairment⁵⁴. In this way therapy and treatment could be tailored by selecting from a range of valid interventions those which are most likely to benefit the individual.

Stinear et al (2007, 2010, 2012)^{54;115;116}, have completed some work on this in the acute stage after stroke. They used a combination of analysis of shoulder and finger movements (SAFE score), TMS measures, fMRI, and diffusion tensor imaging (DTI) to develop an algorithm for selecting individual rehabilitation strategies based on the prediction of functional potential. Further work is required regarding the PREP algorithm proposed in Stinear et al.’s work; however this could be used to as a basis to stratify acute patients in a larger RCT, comparing normal therapy to robotics.

9.4.8 WHAT RESOURCES ARE REQUIRED IN TERMS OF TRAINED AND UNTRAINED STAFF?

The use of robotics devices as an adjunct in upper limb rehabilitation has emerged as an innovative means of delivering quality therapy without increasing staffing capacity or service costs¹⁶². However, little work has looked at the cost implications of using robotic devices in the clinical setting. Wagner et al (2011)²²⁹ is currently the only study that has looked at the cost impact of the use of a robot. They found that the average cost of delivering both intensive comparison therapy and robotic therapy was more expensive than normal care. The cost of both intensive therapy and the use of the device were comparable.

This pilot RCT found that rehabilitation assistances were able to provide supervision of the robotic sessions with weekly checks by a skilled therapist. This is a preliminary indicator for future cost analysis. Cost analysis of the use of device in comparison to normal conventional treatment would need to include: the cost of the machine itself, training staff to use the robot, therapy time required to monitor participants progress on the device, maintenance, cost of fixing the device, and engineering time if it does need repairing .

A debate in the robotic literature has revolved around whether the expensive actuator (motor) components of the robot devices are necessary for the therapeutic effects associated with use of a robot ²³⁰. Recent literature has examined the use of smaller portable devices, which are either non actuated, or EMG triggered ³⁶⁷ , allowing them to be cheaper. Page et al (2013)³⁶⁷ compared the cost of commercially available robotic devices such as InMotion device ,which is in the range of \$75,000, with their EMG triggered device “Myomo” costing \$7,500. This work is still very much in its infancy. In the studies described in this thesis a mock up of the robot – pReachMAN was devised to look at participant’s ability to interface with the device. This device was portable, and although it would need adapting this device could potentially be used in comparison with the actuated version (ReachMAN itself) to investigate this area further.

9.4.9 DOES THE USE OF DIFFERENT UPPER LIMB OUTCOME MEASURES THAT LOOK AT PATIENT FUNCTION BETTER REVEAL ANY ACTIVITY AND PARTICIPATION BENEFIT WITH ROBOTIC DEVICES?

Few of the clinical trials that have investigated the use of robotic in the people with arm difficulties following stroke have incorporated activity and participation level outcome measures in their studies. Liao et al (2011)¹⁸⁶ study is one of the few studies that have used activity and participation outcome measures to look at functional gains with the use of a robotic device. This study found that the group who used the robot appeared to

incorporate their affected arm more in daily tasks than the control group and found the robot group reported significant difference in ability to use their arm when completing the ABILHAND (a patient reported outcome measure). In constant a study by Reinkensmeyer et al (2012)¹⁹⁰ using the Pneu -WREX robot did not find functional improvements on the Motor Activity Log.

The RCT described in this thesis found statistical significant change with using the robot in the ABILHAND (similar to the Liao et al (2011) ¹⁸⁶ study) and trends for improvement with function were also seen in other activity and participation measures used in the trial (CAHI and DASH). Further larger studies would however be required to see if these trends were of significance.

One aspect that was not assessed in the studies was the participants' actual use of their hand and arm in daily life. Accelerometers were used in the Liao et al(2011) ¹⁸⁶ study, and have been used in other studies in an attempt to quantify the amount that people move their arm after stroke (e.g. Lang et al, 2007¹²⁹). Accelerometers have some limitations and one source of unreliability may be that trunk movement can cause passive upper limb movement that may then be recorded as upper limb activity. Additionally, although upper limb movement may be recorded, no information will be provided as to whether the movement was intentional or not, and if it was functional. Lang et al (2007)¹²⁹ however reported good correlation between movements as recorded using an accelerometer and Functional Independence Measure (FIM) scores, suggesting that it may provide an indication of the functional use of the arm. Whilst, accelerometers and the ABILHAND score found increased arm use following the use of the Bi-Manu-Tract robot in ten chronic stroke patients¹⁸⁶

Other studies^{199;190} have used the Motor Activity Log. This scale also measures participants' actual use of their hand and arm in daily life. Ashford et al (2008)²¹⁴ in their systematic review of outcome measures found this measure to be a robust measure of upper limb function. They however found, as did the systematic review carried out in Chapter Four that this measure has psychometric flaws³⁰⁶. It was due to these psychometric flaws that the measure was not used in this study. However it may have been a useful inclusion as a means of looking at the subject's actual use of their impaired upper limbs.

9.4.10 BATTERY OF OUTCOME MEASURES USED IN THE STUDY

The battery of outcome measures used in the study has been found to be valid and reliable in the stroke population. However on analysis of targeting and acceptability, marked floor and ceiling effects were found in the measures.

The outcome measures used to assess changes within the trial population may not have been sensitive enough to detect clinically significant differences within the severely impaired population and the mildly impaired population. Ashford et al(2008)²¹⁴ in their review of upper limb measures echo this view commenting that there is a scarcity of validated tools to assess passive and lower level arm function. Subjects with severely impaired arms who were interviewed regarding using the robotic device remarked that they thought following treatment they were able to use their impaired arms for more functional activities such as holding a page of a book to stabilize while turning the pages, placing a book under their impaired arm to carry it. Marked ceiling was also found with the measures for the subjects with mild arm impairments.

Ashford et al (2013)³⁶⁸ have developed an outcome measure the ArmA that looks at both active upper limb movement and also "passive" *function* (making it easier to care for the

limb (e.g. maintain hygiene) if no motor return is possible. This may be a useful measure to include in future trials when looking at subjects with severely impaired arms. However the measure does not look at items such as the ease in using the affected hand to holding a page of a book (such as described by participants in the interviews in Chapter Seven).

There is a requirement for psychometrically robust instruments capable of reflecting clinically important change in clinical and research practice to cover the full range of upper limb impairments^{214;306}. Particularly there is a need for more sensitive measures of change in those with more severe levels of impairment. Developing a new outcome measure using both tradition and newer psychometric methods (such as Rasch analysis) would address this gap.

9.5 SUMMARY OF LIMITATIONS IN THE STUDIES

The studies described in this thesis comprised of modeling, phase 11 studies which investigated the acceptability, the likely rate of recruitment and retention of subjects and the calculation of appropriate sample size (as described in the feasibility and piloting stage of the MRC framework for complex interventions²³⁸). Therefore no firm conclusions can be drawn from the studies described.

The studies were hampered by small sample numbers, heterogeneous subject groups, lack of blinding, no follow-up period, not matched comparator groups, no record of the exact treatment in the conventional therapy group and problems with the targeting and acceptability of the outcome measures.

9.6 FUTURE WORK

The present study has been able to answer some of the questions raised and gaps identified in the evidence base regarding the use of robotic devices. However it has also identified a wide range of areas that would merit further study. The MRC guidance ²³⁸ provides a framework in which interventions can be tested. This approach is supported by Dobkin (2009) ²⁰⁹ who proposes a progressive series of pilots, prior to larger-scale trials. With this in mind, further pilots investigating the potential benefits of ReachMAN could look at:

- 1) Newer upgraded version of the device, which allows self directed practice
- 2) Different intensity and dose of using the device (i.e. its use over seven days a week, twice daily)
- 3) Comparing the use of ReachMAN with an non actuated device such as pReachMAN
- 4) Looking at the use of ReachMAN in different stroke populations, such as the chronic stroke populations.
- 5) Cost data of the use of a robotic device compared to conventional therapy is required. In an increasingly financially pressured NHS this cost data will be essential for any recommendations for nationwide provision of robotic devices in clinical settings.
- 6) It would be beneficial to perform a definitive RCT using the data from the pilot study to allow definitive conclusions as to the potential benefits of the novel device on arm recovery.
- 7) As discussed the results from both the qualitative and quantitative data imply that the battery of outcome measure used were ineffective in capturing change in arm

function. Future work to develop an outcome measure that can capture change in patients with severe arm impairment would be extremely beneficial.

9.7 CONCLUSION

Stroke is a significant cause of disability in the population. When the hand and arm are affected by stroke, functional recovery may be poor. There is a range of factors that affect the upper limb after stroke and impact on recovery. The mechanisms by which recovery occurs remain unclear; although, repetitive task-specific training appears to be beneficial. The use of robotic devices as an adjunct to rehabilitation of the arm post stroke has emerged as an innovative means to deliver repetitive arm movements. Although, there is evidence to suggest that the use of robotic devices may have beneficial effects on upper limb recovery after stroke, there remain unanswered questions regarding the use of this intervention. This is particularly apparent regarding the translation of rehabilitation robotics from research into clinical practice.

This thesis aimed to bridge between research and clinical utilisation of a robotic device. It is difficult to evaluate 'complex interventions', such as rehabilitation. Appropriate outcome measures that are valid, reliable and sensitive are required. Initially a systematic review looking at upper limb outcome measures found that the STREAM, CAHAI, ABILHAND, FMA, ARAT, EQ5D, Barthel index, NIHSS and DASH were the most appropriate measures to use to evaluate the use of a robotic device in sub acute strokes.

A recruitment study found that out of 125 subjects, of the people who had upper limb difficulties, almost half were able to use the robotic device. A subsequent pilot RCT found statistical significant change in one of measures used ABILHAND, but not the primary outcome measure the FMA. . The efficacy of using the device in comparison to subjects

normal therapy was therefore not proven in a sub acute stroke population. However as well as one measure showing statistical significance, there was a trend towards improvement in motor performance and function in the robotic group. The trial demonstrated that, even amongst the severely impaired stroke population, there can be improvement in motor performance. Subjects were only able to tolerate 20 minutes use of the device due to participant fatigue. Limitations of the study related to the sensitivity of the outcome measures to assess change within this population; the absence of blinding in the study; no matched intensity of therapy in the control group to that in the intervention group.

Interviews with subjects found that they described a positive impact of using the device on function and movement in their arm and it to be motivating and enjoyable. They wished to be able to use it independently and reinforced that they found 20 minutes the maximum amount of time they could use the device for. Problems were seen with the targeting and acceptability of the battery of outcome measures, while use of Rasch analysis allowed deeper analysis of the measures and also suggestions on how to improve the measures for future use.

In summary, further work is required to investigate therapeutic interventions for the upper limb in all phases of stroke recovery, and specifically the use of robotic devices. Although the null hypotheses were not rejected the trends seen with use of the device, support further investigation into the use of REACHMAN in the stroke population. This work should identify appropriate ways of measuring changes that are clinically important and meaningful for individuals with stroke.

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APPENDIX 1 CONVENTIONAL UPPER LIMB PT / OT TREATMENT RECORDING FORM

Conventional Upper Limb PT / OT Treatment Recording Form

Date: Patient ID: Therapist ID:

Individual treatment session Y/N Upper limb group Y/N 1:1 Y/N

No. PT(s) used: No. OT(s) used: Number rehab assistant(s) used:

Estimated duration of UL Rx: Aim of session:

Postural set(s) utilised: Stand.... Sit.... Supine.... Prone standing.... Side lying....Other.....

Setting: Gym:..... Ward:.... Bathroom:.....Kitchen:.....Home environment..... Work environment:....

Equipment used:

Treatment Activities:

- 1.0 *Soft tissue mobilisation / realignment* ☐
2. 0 *Joint mobilisation* ☐
- 3.0 *Hand oedema management* ☐
- 4.0 *Facilitation of muscle activity / movement* ☐
- 5.0 *Sensorimotor integration*
- 5.1 Tactile stimulation and muscle activation ☐
- 5.2 Proprioceptive stimulation and muscle activation ☐
- 5.3 Electrical stimulation and muscle activation ☐
- 6.0 *Strengthening*
- 6.1 Resistance from therapist ☐
- 6.2 Resistance from body weight ☐
- 6.3 Resistance from object weight ☐
- 7.0 *Task orientated training*

7.1	Reach to grasp with facilitation	<input type="checkbox"/>
7.2	Reach to grasp without facilitation	<input type="checkbox"/>
7.3	Manipulation	<input type="checkbox"/>
7.4	Bimanual task with facilitation	<input type="checkbox"/>
7.5	Bimanual task without facilitation	<input type="checkbox"/>
8.0 <i>Balance and mobility tasks incorporating upper limb activity</i>		
8.1	In or from lying	<input type="checkbox"/>
8.2	In or from sitting	<input type="checkbox"/>
8.3	In or from standing	<input type="checkbox"/>
8.4	In walking	<input type="checkbox"/>
9.0 <i>Positioning</i>		
9.1	In bed	<input type="checkbox"/>
9.2	In armchair	<input type="checkbox"/>
9.3	In wheelchair	<input type="checkbox"/>
10.0 <i>Seating</i>		
10.1	Anti-sag in situ	<input type="checkbox"/>
10.2	Scaffolding of pelvis	<input type="checkbox"/>
10.3	Trunk support	<input type="checkbox"/>
10.4	Tray	<input type="checkbox"/>
10.5	Other	<input type="checkbox"/>
11.0 <i>Splinting /taping</i>		
11.1	Shoulder	<input type="checkbox"/>
11.2	Elbow	<input type="checkbox"/>
11.3	Wrist / hand	<input type="checkbox"/>
12.00 <i>Education for patient and/or carer</i>		

2010

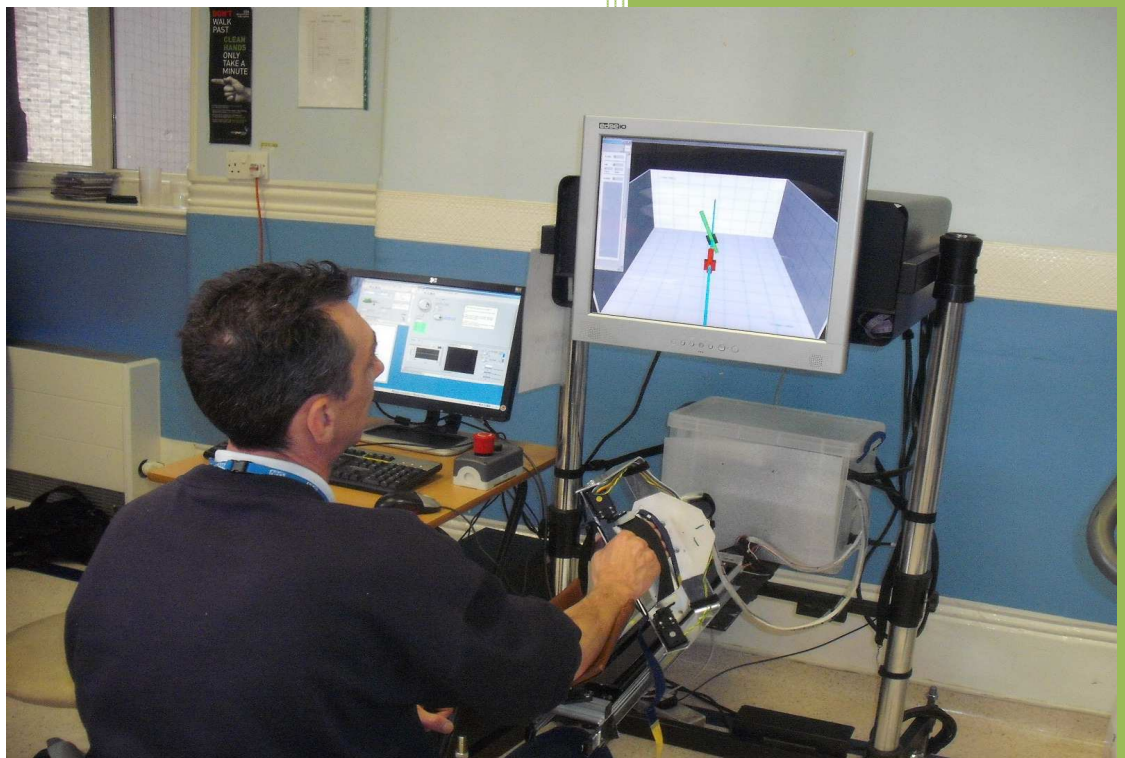
12.1 Self monitoring of UL

12.2 Assistance with stretches

2.3 Assistance with transfers

Instruction Manual for ReachMAN

APPENDIX 11 REACHMAN PROTOCOL



SUMMARY

SWITCH ON

1. Switch on computer with password '**1234**'
2. Open **ReachMAN.lvproj** → open both **host.vi** and **target.vi**
3. Click run (white arrow) on the **HOST.vi** first.
 - a. 3D window will pop out and adjust it to the other monitor.
4. Click run (white arrow) on the **TARGET.vi** and make sure the robot is in safe position.
5. Change the **name and date** as required on the TARGET.vi interface.

INITIALIZATION

6. Robot is ready to go and first step is to INITIALIZE the robot position.
 - a. Go to host.vi and select '**INIT**' (default setting).
 - b. Choose required **left or right hand**.
 - c. Make sure robot is in good position – around in the middle of the linear guide and the grasping is in close position.
 - d. Click the **START** button
 - e. Robot should move. If not, check the emergency button if it's switched off.
 - f. Do not touch the robot while moving.
 - g. When the robot stop completely, manually adjust the 'rotation' and then click on the '**Reset Rot**'.
7. Now can place patient to the robot. Adjust the ideal comfortable position for the patient. Make sure the shoulder is parallel with body trunk and elbow flexed to about 90° and the robot position should be at initial position (mark by a marker)
8. Position with trunk restraint.
9. Select Game and select one of the **four different modes** to play; Reaching, Pronosupination, Grasping and Combination. Select the appropriate level and make sure to click the '**Reset Level**' each time the level is changed.

TREATMENTS

10. Treatment should start with reaching, pronosupination, grasping and finally combination. Perform about 5 on each one. Only train combination if patients are able to perform in more than level 2 for reaching and pronosupination. Skip the exercise if patient could not do it.
11. In the first session, level should start from lowest or based on the performance from assessment. The next day session's level should follow the previous session.
12. One Level increased when patient is able to score perfect 10 with score more than 90% for three consecutive exercises. Only 1 level increment per session.
13. When treatment is finish, stop the program by pressing the ESC button. This will close the program properly and save all the required data.
14. The data is saved at ftp://192.168.0.40/data/.

ASSESSMENT

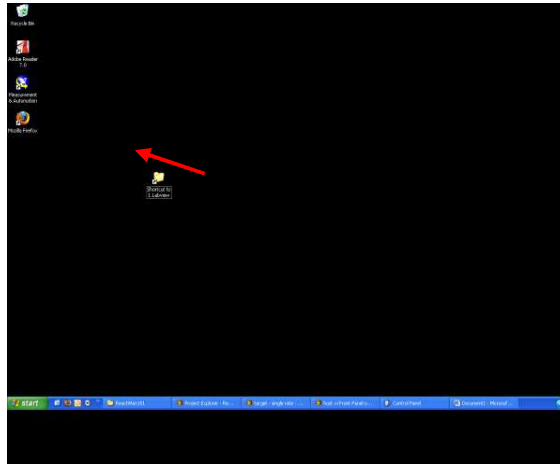
15. Assessment is done on the second and last sessions. Two measurements are done here which are the forces and score on each exercise.
 - a. FORCE measurements

Choose both the '**AUTO ASSESS**' and '**Reaching**' together. Measure pushing&pulling forces and pronation&supination torques. Ask the patients to perform each of the four movements as hard as possible for about 3 seconds and twice on each one.
 - b. PERFORMANCE of exercises

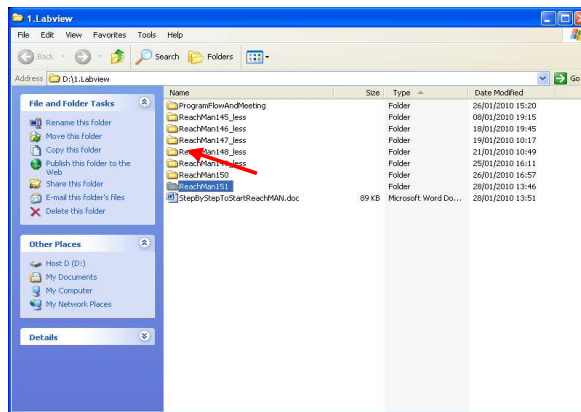
Train at least twice on **level 7** for reaching, pronosupination and grasping.

Step by step Guidance to operation

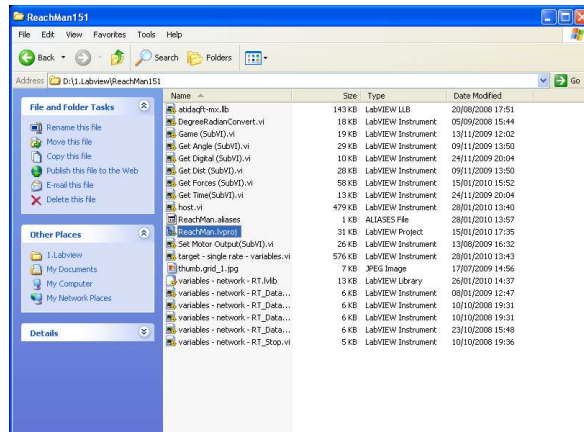
1. Switch on computer and enter password '1234'
2. Click on the ReachMAN.lvproj shortcut in the desktop and proceed to step 5. If click onto folder 'Shortcut to 1.Labview' on the screen, then proceed to step 3.



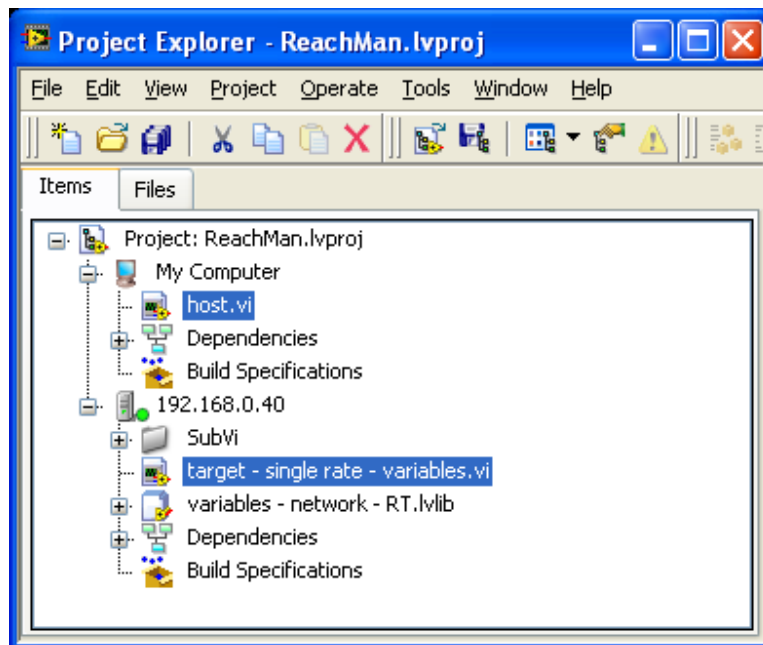
3. Select the most recent ReachManNUM folder with NUM is the most recent number. The software is updated regularly and the most recent program is updated with the highest NUM number. In the screenshot below, the most recent one is ReachMan151.



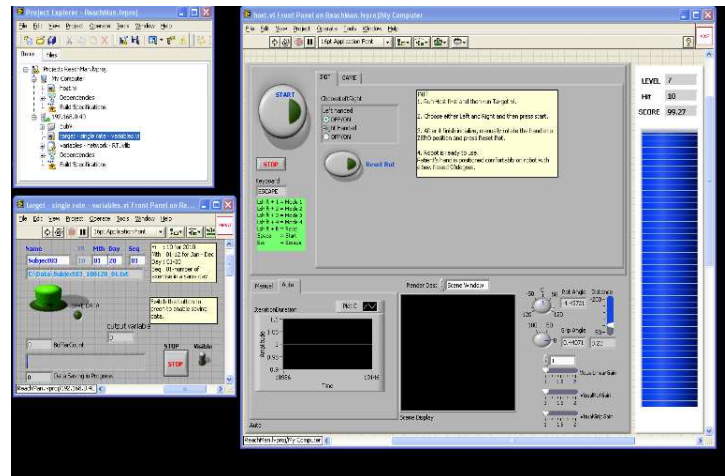
4. Choose and open ReachMan.lvproj.



- Double click and open **host.vi** and **target-single rate-variables.vi**:

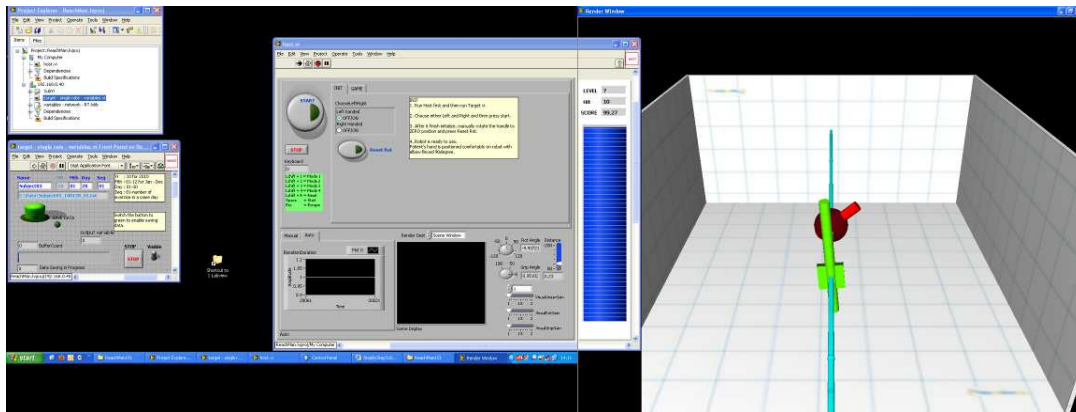


6. Your computer screen should look like this. The right is your HOST VI (Virtual Instrument) and bottom left is the VI for target (the robot)

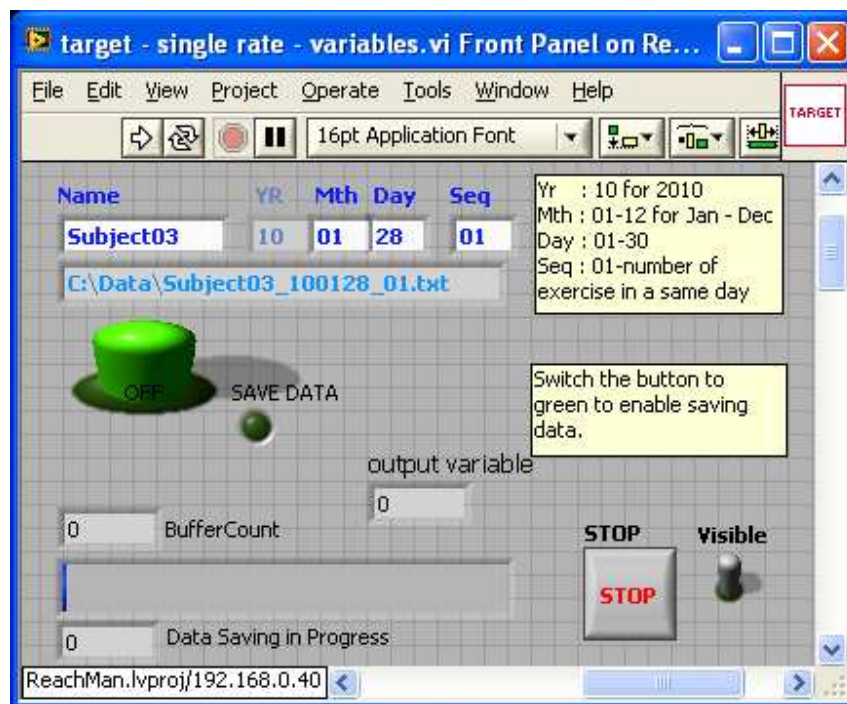


7. Click play on the host (the arrow on top left). Once it's running, you will have a window screen showing 3D visual pop up. Drag and enlarge the screen on the second monitor

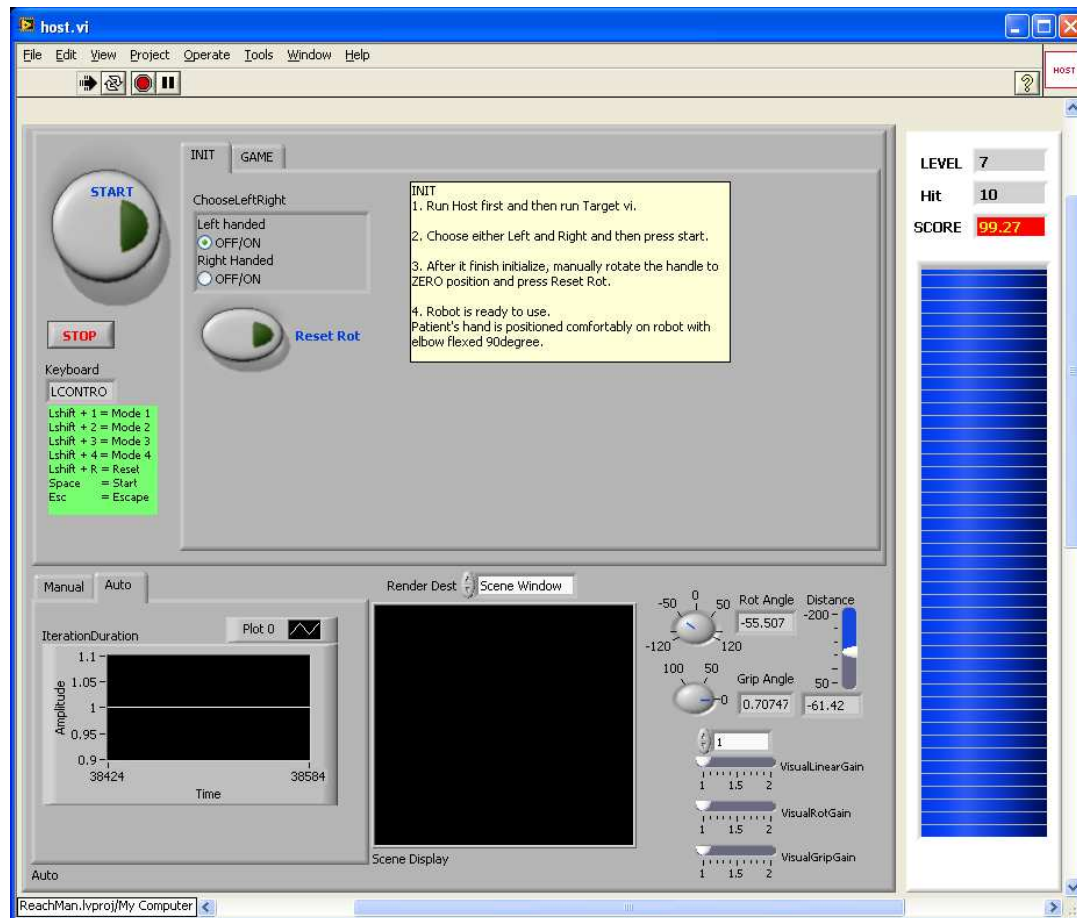
as it's shown below. Adjust the Host.vi position so the score and the big blue progress bar is overlapping a small part of the leftmost of the 3D window screen **so patient can see both the 3D visual and the score.**



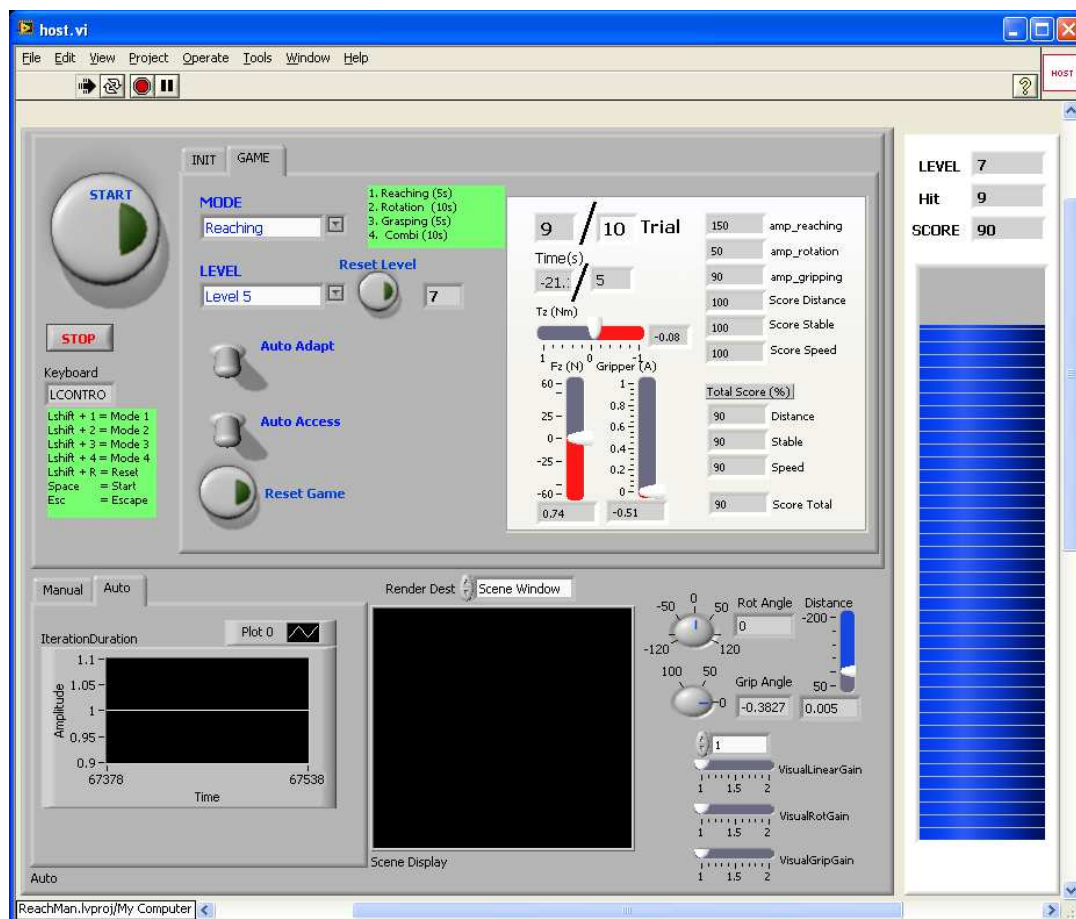
8. Now, click run on the target (the arrow on the top left). Write the Name of the subject, Month, Day and Seq for naming a filename to be saved. You can do this before or after running the target. Example below shows the filename is Subject03_100128_01.txt. All files are saved in C:\Data.



9. Once you done that, go to **INIT** bar (default) and then choose which hand to exercise. Then, click the **START** and press the '**green**' button on the emergency button. Make sure the robot grasping mechanism is fully closed and the robot is at about the central position. The robot should move on it's own to initialise its position. (*do not touch or block the robot's way during the initialise movement*).The robot starts to move backward linearly and then rotate anti clockwise until reaching the limit. Then, the robot will move to start position for both linear (labelled with a yellow sticker) and rotation clockwise to zero degree for chosen left or right hand. Make adjustment manually on the rotation to exactly vertical position and click '**Reset Rot**'. Press the emergency's red button if robot has to be stopped.



10. Position patient to robot handle and wrap as required. Height of the robot is adjusted so the elbow and hand are placed nicely on the arm support.
11. Click on the game bar where you can select what exercise mode to choose and which level to start with. There are 4 exercise modes to choose which are reaching, pronosupination, grasping and combination. There are 9 levels on each exercise. Make sure to click on the '**Reset Level**' to submit the changes each time the level is required to modified. You have to do this individually on each of the mode.



12. Choose desired exercise's mode and level, and then click **Start**. Patient has to move the handle (shown as green object) to match the target (red object). Each start has 10 targets to reach and patient progress is shown as number of **hit** and **score**. The score is inclusive of progress in movement, speed and stability.
13. Once they finish the experiment, double check with the filename again and then press **Esc** or click on the **STOP** button (below Start button) on the Host.vi. (do not use other possible ways to stop the program as that will cause the program not to save the data correctly).
14. Data are saved at <ftp://192.168.0.40/Data/> and can be retrieved either using windows explorer or any internet browser.

POSITIONING THE PATIENT

Adjust the ideal comfortable position for the patient.

- Make sure the shoulder is parallel with body trunk
- Elbow flexed to about 90° and the robot position should be at initial position (mark by yellow marker)
- Ensure patient is sat well in chair/wheelchair.



USING TRUNK RESTRAINT

This is to prevent excessive trunk movement; ensuring movement is from the arm.

- Place two folded towels into a pillowcase
- This forms an abdominal pad (place pillow cases on subjects abdominals)
- Secure in place with a sheet
- Tie at back of chair.





APPENDIX 111 PSYCHOMETRIC EVALUATION CRITERIA WITH DEFINITIONS

Psychometric evaluation criteria with definitions

<p>Content validity. The extent to which the domain of interest is comprehensively sampled by the items in the measure</p> <p>1) Patients were involved during item selection and/or item reduction.</p> <p>2) Patients were consulted for reading and comprehension.</p> <p>Rating:</p> <p>+ patients and (investigator or expert) involved</p> <p>± patients only</p> <p>– no patient involvement</p> <p>? no information found on content validity</p>	<p>Floor and ceiling effects. The measure fails to demonstrate a worse score in patients clinically deteriorated and an improved score in patients who clinically improved</p> <p>1) Descriptive statistics of the distribution of scores were presented.</p> <p>2) 15% of respondents achieved the highest or lowest possible score.</p> <p>Rating:</p> <p>+ no floor/ceiling effects</p> <p>– more than 15% in extremities</p> <p>? no information found on floor and ceiling effects</p> <p>Test-retest reliability. The extent to which the same results are obtained on repeated administrations of the same questionnaire when no change in physical functioning has occurred</p>
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<p>Internal consistency. The extent to which items in a (sub)scale are intercorrelated;a measure of the homogeneity of a (sub)scale</p>	<p>1) Calculation of an intraclass correlation coefficient (ICC); ICC > 0.70.</p>
<p>1) Factor analysis was applied in order to provide empirical support for the dimensionality of the questionnaire</p>	<p>2) Time interval and confidence intervals were presented.</p>
<p>2) Cronbach's alpha between 0.70 and 0.90 for every dimension/subscale</p>	<p>Rating:</p>
<p>Rating:</p>	<p>+ adequate design, method, and ICC > 0.70</p>
<p>+ adequate design & method; factor analysis; alpha 0.70–0.90</p>	<p>± doubtful method was used</p>
<p>± doubtful method used</p>	<p>– inadequate reliability</p>
<p>– inadequate internal consistency</p>	<p>? no information found on test-retest reliability</p>
<p>? no information found on internal consistency</p>	<p>Agreement. The ability to produce exactly the same scores with repeated measurements</p>
<p>Construct validity. The extent to which scores on the measure relate to other measures in a manner that is consistent with theoretically derived hypothesis concerning the domains that are measured.</p>	<p>1) For evaluative questionnaires reliability agreement should be assessed.</p>

<p>1) Hypotheses were formulated.</p> <p>2) Results were acceptable in accordance with the hypotheses.</p> <p>3) An adequate measure was used.</p> <p>Rating:</p> <p>+ adequate design, method, and result</p> <p>± doubtful method used</p> <p>– inadequate construct validity</p> <p>? no information found on construct validity</p> <p>Responsiveness. The ability to detect important change over time in the concept being measured</p> <p>1) For evaluative questionnaires responsiveness should be assessed.</p> <p>2) Hypotheses were formulated and results were in agreement.</p>	<p>2) Limits of agreement, Kappa or standard error of measurement (SEM) presented.</p> <p>Rating:</p> <p>+ adequate design, method and result</p> <p>± doubtful method used</p> <p>– inadequate agreement</p> <p>? no information found on agreement</p> <p>Interpretability. The degree to which one can assign qualitative meaning to quantitative scores</p> <p>Authors provided information on the interpretation of scores:</p> <p>1) Presentation of means and standard deviation of scores before and after treatment.</p>
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<p>3) An adequate measure was used (effect size (ES), standardized response mean (SRM), comparison with external standard).</p>	<p>2) Comparative data on the distribution of scores in relevant subgroups.</p>
<p>Rating:</p>	<p>3) Information on the relationship of scores to well-known functional measures or clinical diagnosis.</p>
<p>+ adequate design, method and result</p>	<p>4) Information on the association between changes in score and patients' global ratings of the magnitude of change they have experienced.</p>
<p>± doubtful method used</p>	<p>Rating:</p>
<p>– inadequate responsiveness</p>	<p>+ 2 or more of the above types of information was presented</p>
<p>? no information found on responsiveness</p>	<p>± doubtful method used or doubtful description</p>
<p>Minimal clinically important difference (MCID). The smallest difference in score in the domain of interest which patients perceive as beneficial and would mandate a change in patient's management. Information is provided about what (difference in) score would be clinically meaningful.</p>	<p>? no information found on interpretation</p>
<p>Rating:</p>	<p>Time to administer. Time needed to complete the questionnaire</p>
<p>+ MCID presented</p>	<p>Rating:</p>

<p>– no MCID presented</p> <p>Administration burden. Ease of the method used to calculate the questionnaire's score</p> <p>Rating:</p> <p>+ easy: summing up of the items</p> <p>± moderate: visual analogue scale (VAS) or simple formula</p> <p>– difficult: VAS in combination with formula, or complex formula</p> <p>? no information found on rating method</p>	<p>– more than 10 min</p> <p>+ less than 10 min</p> <p>? no information found on time to complete the questionnaire</p>
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Measure	Time	Administrative Burden	Content Validity	Internal consistency	Construct validity	Floor/ceiling effect	Reliability	Agreement	Responsiveness	Interpretability	MCID
ABILHAND	–	+	+	+	+	–	+	+	+	+	+
CAHAI	-	+	+	+	+	-	+	+	+	+	?
STREAM	+	+	+	+	+	-	+	?	+	?	?

MCID: minimal clinically important difference; method or result was rated as: + adequate; ± doubtful; – poor; ? no data available;

APPENDIX 1V-CONSENT AND INFORMATION SHEET FOR PHASE 1

Date 17th June 2008

Centre Number:

08/0107

Patient Identification Number for this study:

UCLH Project ID number:

Form version: 2

CONSENT FORM

Title of project: A feasibility study of use of a cheap, portable robotic aid for delivering repetitive practice of reach, supination, and manipulation in acute stroke: Phase 1

Name of Principal Investigator: Dr ED Playford

Name of Research Physiotherapist: Karen Baker

Please initial box

1. I confirm that I have read and understood the information sheet dated
(version) for the above study and have had the opportunity to ask
questions.

☐

2. I confirm that I have had sufficient time to consider whether or not want to
be included in the study

☐

3. I confirm that I am happy for my general practitioner to be informed of my
participation in this study

☐

4. I understand that my participation is voluntary and that I am free to withdraw
at any time, without giving any reason, without my medical care or legal
rights being affected.

☐

5. I understand that sections of any of my medical notes may be looked at by
responsible individuals from (company name) or from regulatory authorities
where it is relevant to my taking part in research. I give permission for these
individuals to have access to my records.

☐

6. I agree to take part in the above study.

☐

Continued on next page

1 form for Patient;
1 to be kept as part of the study documentation,
1 to be kept with hospital notes

Centre Number:
08/0107

UCLH Project ID number:

Patient Identification Number for this study:

Form version: 2

CONSENT FORM

Title of project: A feasibility study of use of a cheap, portable robotic aid for delivering repetitive practice of reach, supination, and manipulation in acute stroke: Phase 1

Name of Principal Investigator: Dr ED Playford
Name of Research Physiotherapist: Karen Baker

_____	_____	
Name of patient	Date	Signature

_____	_____	
Name of Person taking consent (if different from researcher)	Date	Signature

Karen Baker	k.baker@ucl.ac.uk	t: 0845155500 x 723821
Researcher (to be contacted if there are any problems)	Email/phone number	

Comments or concerns during the study

If you have any comments or concerns you may discuss these with the investigator. If you wish to go further and complain about any aspect of the way you have been approached or treated during the course of the study, you should write or get in touch with the Complaints Manager, UCL hospitals. Please quote the UCLH project number at the top this consent form.

1 form for Patient;
1 to be kept as part of the study documentation,
1 to be kept with hospital notes

APPENDIX V-- ETHICS APPROVAL AND ADMENTS TO ETHICS APPROVAL

The National Hospital for Neurology and Neurosurgery & Institute of Neurology Joint REC

Dr Diane Playford

REC Office

South House

National Hospital for Neurology and Neurosurgery

Royal Free Hospital

Queen Square

Pond Street

London

London

WC1N 3BG

NW3 2QG

Tel: 020 7794 0500 ext. 31342

Our Ref 09L 476

Fax: 0207 7941004

Email:

Sasha.Vandayar@royalfree.nhs.uk

Website: www.uclh.nhs.uk

02 December 2009

Dear Dr Playford

Study title: A feasibility study of use of a cheap, portable robotic aid for delivering repetitive practice of reach, supination, and manipulation in acute stroke

REC reference: 08/H0716/13

Amendment number: 1

Amendment date: 05 November 2009

The above amendment was reviewed at the meeting of the Sub-Committee held on 02 December 2009.

Ethical opinion

The members of the Committee taking part in the review gave a favourable ethical opinion of the amendment on the basis described in the notice of amendment form and supporting documentation.

Approved documents

The documents reviewed and approved at the meeting were:

Document	Version	Date
Protocol	2	30 September 2009
Notice of Substantial Amendment (non-CTIMPs)	1	05 November 2009

Membership of the Committee

The members of the Committee who took part in the review are listed on the attached sheet.

R&D approval

All investigators and research collaborators in the NHS should notify the R&D office for the relevant NHS care organisation of this amendment and check whether it affects R&D approval of the research.

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees (July 2001) and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

08/H0716/13: Please quote this number on all correspondence

Yours sincerely

Miss Sasha Vandayar

COMMITTEE CO-ORDINATOR

E-mail: Sasha.Vandayar@royalfree.nhs.uk

Enclosures: List of names and professions of members who took part in the review

Copy to: R&D - UCLH

**The National Hospital for Neurology and Neurosurgery & Institute of Neurology Joint
REC**

Attendance at Sub-Committee of the REC meeting on 02 December 2009

<i>Name</i>	<i>Profession</i>	<i>Capacity</i>
-------------	-------------------	-----------------

Dr Yogi Amin	Consultant in Neuroanaesthesia & Neurocritical Care	Expert
Ms Katy Judd	Consultant Nurse	Expert



APPENDIX V1- - CONSENT FORM AND INFORMATION SHEET FOR RCT

Version 1.
Date 5.03.08
UCLH Project ID number:

Patients information sheet: Part 1

1. Study title

Phase II of A feasibility study of use of a cheap, portable robotic aid for delivering repetitive practice of reach, supination, and manipulation in acute stroke:

2. Invitation

We would like to invite you to take part in a research study. Before you decide you need to understand why the research is being done and what it would involve for you. Please take time to read the following information carefully. Talk to others about the study if you wish. (Part 1 tells you the purpose of this study and what will happen to you if you take part. Part 2 gives you more detailed information about the conduct of the study). Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.

3. What is the purpose of the study?

Following stroke approximately 30% of patients are left with some weakness in the arm. There is growing evidence that increasing use of the arm early after stroke improves outcome. However, augmenting therapy time is difficult. Currently most stroke units have one physiotherapist for every six patients, and patients receive about one hour of therapy each day. To increase therapy time to 4 hours a day would mean that a physiotherapist would have to be employed for every 2 patients. The use of robotic aid is a potential solution to the difficulties in increasing practice time. 'Robotic' aids can provide high-intensity, repetitive, task specific, interactive treatment of the affected arm. The aim of this study is to determine how a robotic intervention would be delivered to patients in a randomised controlled trial. We hope to establish how long it takes to set up the equipment so that a patient can use it, and to establish how often and for how long patients use the device. In addition we want to know how easily the measures we use detect any differences between a group who use the device and a group who do not.

4. Why have I been chosen?

You have been chosen because you have been recently diagnosed with stroke, your arm is affected

5. Do I have to take part?

It is up to you to decide whether or not to take part. If you do decide to take part you will be given this information sheet to keep and be asked to sign a consent form. If you decide to take part you are still free to withdraw at any time and without giving a reason. Decisions to withdraw at any time, or a decision not to take part, will not affect your future medical care.

6. What is involved in the study?

If you agree to take part you will be assigned to one of two different groups. Because we do not know if the robotic intervention will be helpful, we need to make comparisons. You will have a fifty-fifty chance of being in either group A or group B.

One group, group A, will undergo 'usual practice'. They will be provided with physiotherapy and occupational therapy appropriate to their needs as determined by the clinicians looking after them. Typically this would be a physiotherapy session everyday of the week and an occupational therapy session 2 or 3 times each week.

The second group, group B, will be usual practice rehabilitation but in addition they will be asked to practice for at least an hour each day, and for as long as they want to using the robotic aid. They will be asked to continue this practice daily for six weeks. We will record how long you practice for in order to work out what is practical for most patients. We will also ask you about your experience of using the robotic aid.

All patients will have the the function on the affected arm tested at entry to the study and six weeks later using a series of simple tests and questionnaires. The tests will include activities such as lifting blocks or put small pegs into a hole. Each of these assessments will take approximately 45 minutes.

7. What is the procedure being tested?

The procedure being tested is the ability to use 'robotic' aid for repetitive practice. It is not, at present a treatment but may be one in the future.

8. What are the alternatives for treatment?

Currently robotic aids are not in use for routine treatment. All patients who need it will receive physiotherapy and occupational therapy.

9. What are the possible disadvantages and risks of taking part?

The disadvantages of taking part in this study is that it will require time and effort when you may be feeling distressed by what has happened to you. The main risk to those in group B is that

repetitive practice may make your hand, arm, shoulder, neck or back ache. If this happens you should tell the doctors and nurses looking after you at the time, who will be able to give you some pain killers. In addition should tell the research physiotherapist who will advise you about whether you should modify your practice in anyway.

10. What are the possible benefits of taking part?

It is possible that those in the repetitive practice group will get some improvement in arm function greater than that that would have occurred anyway. There is some evidence that this is the case but the evidence is not strong.

11. What if there is a problem?

Any complaint about the way you have been dealt with during the study or any possible harm you might suffer will be addressed. The detailed information on this is given in Part 2.

11 Will my taking part in the study be kept confidential?

Yes. We will follow ethical and legal practice and all information about you will be handled in confidence. The details are included in Part 2.

Patients information sheet: Part 2

12. What if relevant new information becomes available?

Sometimes we get new information about the treatment being studied. If this happens, your research physiotherapist will tell you and discuss whether you should continue in the study.

13. What will happen if I don't want to carry on with the study?

If you decide to withdraw from the study and we have already collected some information about you, you have two choices. Either you can let us use the data that we have already collected or you can ask for it to be destroy

14. What if there is a problem

If you have a concern about any aspect of this study, you should ask to speak to the researchers who will do their best to answer your questions (0845 155500 ext 3166). If you remain unhappy and wish to complain formally, you can do this through the NHS Complaints Procedure Details can be obtained from the hospital.

In the event that something does go wrong and you are harmed during the research and this is due to someone's negligence then you may have grounds for a legal action for compensation against UCLH NHS Foundation Trust but you may have to pay your legal costs. The normal National Health Service complaints mechanisms will still be available to you (if appropriate).

15. Will my taking part in this study be kept confidential?

The information we collect about you will be collected first on paper and then transferring to a computer. When it is transferred to the computer the information will be anonymised and you will be identified by a number unique to this study. The information will be stored on a single computer that is password protected and kept in locked room. Only those people directly involved with the analysis of the information will have access to it. It will not be made available to other people, or for other studies. At the end of seven years the information will be destroyed.

16. Involvement of the General Practitioner/Family doctor (GP)

Your GP and your Consultant will both be informed that you are taking part in the study, unless you prefer that they are not informed.

17. What will happen to the results of the research study?

The preliminary results of the research will be available in the summer/autumn 2010. They will be published in a medical journal the following year. The stroke association will also publish the results of the study through their magazines and websites. You will not be identified in any report/publication.

The final results will be available in 2012 and will be published in a medical journal and via the Stroke Association

18. Who is organising and funding the research?

The Stroke Association is funding the research

19. Who has reviewed the study?

All research in the NHS is looked at by independent group of people, called a Research Ethics Committee to protect your safety, rights, wellbeing and dignity. This study has been reviewed and given favourable opinion by The National Hospital for Neurology and Neurosurgery/Institute of Neurology Joint Research Ethics Committee.

20. Contact for Further Information

If you require any further information please contact Dr Diane Playford, Consultant Neurologist,
on 08



APPENDIX V11 INFORMATION SHEET REGARDING THE INTERVIEWS

RESEARCH PARTICIPANT INFORMATION SHEET

You are being invited to take part in a research study. Before you decide, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish. Ask me if there is anything that is not clear or if you would like more information.

Thank you for reading this

Title of the study:

Patients' and carers' perceptions of the use of robotics in upper limb rehabilitation after stroke.

What is the purpose of the study?

Robotic aids have been introduced to stroke rehabilitation to allow extra practice of arm exercises. Involving patients in the design and planning of therapy programs has been shown make rehabilitation more effective. The aim of this study is to find out how stroke patients and their carers feel about using robotic aids as part of their rehabilitation. In particular it will look at aspects of design, ways in which it is used, and means of improving motivation to participate in therapy.

Physiotherapy will not be provided as part of this study. The study is about obtaining your views on robotic therapy. It is hoped that the information you provide will influence the development of future robotic aids and therapy programs.

Why have I been chosen?

You have been approached because you or your relative have experience of using a robotic aid as part of your stroke rehabilitation program at the National Hospital for Neurology and Neurosurgery. You are the best person to describe your experience of using the robotic aid.

Do I have to take part?

No, participation is entirely voluntary. You are under no obligation to take part in this study. If you decide to participate and then at some point change your mind **you are free to withdraw from the study at any point and do not need to give a reason for doing so.** Declining to take part will not impact on any services you are currently receiving or may receive in the future.

What will happen to me if I take part?

If you are considering taking part or would like to know more about the study you can either phone me on the number listed below or you can speak to Karen Baker, the research physiotherapist at the National Hospital for Neurology and Neurosurgery. We can then explain the study to you and answer any questions you might have. If you are willing to participate in the study then I will arrange a convenient time to visit you in your home to conduct an interview to obtain your views on this topic. The interview may take as long as an hour, although this length of time may not be required and some interviews will be shorter. I will need to tape record our conversation so that I am able to remember all the points you make accurately.

Will my taking part be kept confidential?

All information and data obtained from you will be treated as privileged and confidential. It will be stored in a secure area and not released to any unauthorised person without your permission. The consent form will be the only document that has your full name on it and it will be stored safely and separately from the other data. When the information is written up I may use direct quotes but you will not be identifiable from them.

What are the possible benefits of taking part?

The benefit of you taking part in this study is that your opinion, together with the opinions of the other participants, will hopefully help to influence and inform the development of a new robotic aids and rehabilitation programs for other stroke survivors.

What are the risks in taking part?

It is possible that you may become upset when talking about your stroke and rehabilitation. If I feel concerned about your well being because of how unhappy you are feeling then I would need to break confidentiality and discuss this with your doctor. I would let you know if I was going to do this.

What will happen to the results of the study?

The information received from you and the other participants will be used to write an MSc (Neurorehabilitation) dissertation project. The results will be presented to healthcare professionals and engineers who are interested in the development of robotic therapy.

Concerns and Complaints

Any queries regarding the project can be directed to the research supervisor, her details are listed below. If at any point during the study you have any concerns or complaints about the study or the student these can be addressed to the Chair of the Research Ethics Committee. Contact details have been listed below.

Thank you very much for taking the time to read this information. If you have any questions please do not hesitate to ask me or you can contact me on the number below.

My Contact Details:	My Supervisor's details:
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<p>Brid Spillane</p> <p>MSc Neurorehabilitation, School of Health Sciences & Social Care Brunel University, UB8 3PH</p> <p>Tel: 07910344963 Email: om09bbs@brunel.ac.uk</p>	<p>Dr Sally Spencer</p> <p>Lecturer in Health Studies School of Health Sciences & Social Care Brunel University, UB8 3PH</p> <p>Tel: 01895 268843 Email: sally.spencer@brunel.ac.uk</p>
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Chair of the Research Ethics Committee

Elizabeth Cassidy
School of Health Sciences and Social Care
Brunel University UB8 3PH
Tel: 01895 268736
elizabeth.cassidy@brunel.ac.uk

Research ethics approval has been obtained from the School of Health Sciences and Social Care Research Ethics Committee and the Joint Research Ethics Committee of The National Hospital for Neurology and the Institute of Neurology.



APPENDIX V111- INTERVIEW TOPIC GUIDE

- Check that the participant is still happy to be involved in the research
- Check that participant is OK with being recorded. Reassure about confidentiality.
- Reminder of the purpose of the interview. Indicate length of interview.

Tell me about your experience of using the robot?

General perceptions of robot and expectations.

Prompts: Expectation
 Comfort
 Pain
 Satisfied
 Safe
 Confusing

Perceptions of the treatment protocol.

Prompts: Too long, too short
 Challenging
 Meaningful/Functional
 Any changes

Design of robot

Prompts Appearance
 Comfort
 Ease of setting up and attachment
 Any changes?

Motivational Aspects?

Prompts: Help with motivation to persist with practice?
Feedback:
 Helpful?
 Understandable?
 Sufficient?
Computer games:
 Opinion on using computer games in stroke rehabilitation
 Enjoyable? Interested?
Virtual Reality

Use of Robot in Different Environments

Prompts: Using the robot at home:
 Barriers (assistance, size etc)

Benefits
Outpatient setting
Telerehabilitation

Is there anything else you would like to tell me about your experience of the robot?

Thank the participant



APPENDIX V1V-EXAMPLE OF FRAMEWORK ANALYSIS CARRIED OUT ON INTERVIEW TRANSCRIPTS.

Robotic Arm interviews

I can leave that between us. I have got some questions that I have asked everybody

Ok

So that I get the same general ideas from everybody. So the first one is so broad and general, can you tell me about your experience of using the robot?

Ah well, first of all my experience of using it. I think at first I didn't see or feel like I needed to do this because I thought it wasn't helping so when I heard about the robot I thought it was just something that would do the actual thing for you.

Yes

But then, it is not bad. I mean it is coming. Gradually I am getting to, you know, sort of like and to actually use it. I try to go to the sessions more often.

Ok

At first I was just a bit senseless and just could not be bothered, couldn't be asked to do anything.

Whereas have you found that it has been a bit helpful for you?

I think it does because, I think, yeah it does. Because it has been helping me a lot with my reaching and stuff ok?

(Agrees)

Although my hand is not you know, my grasping is not as 100% it does help.

What did you, what was your first impression of it when you saw it the first time?

As I said at first my first impression when I heard of the term robot was not going to be, I thought it was actually a (pause) programmed machine that actually does something for you like, basically it is programmed to do the actual action. But when I saw it I was like "Ok this is actually a computer, actually it is, you know, set and runs the programme as one"

And you can interact with it

Interact with it, hands on.

That is good about it isn't it? What do you think about the idea of using robotics in stroke rehab?

Actually it is a good idea but I just had one kind of...maybe I shouldn't say wish. I was just hoping that it would have been more easier to use.

Ok

Yes

Yes

And maybe benefits are more obvious because I didn't really get it at first, to be honest.

I think that is fair enough. In terms of it being easier to use, do you mean easier to get yourself set up on it?

Yes user friendly as well and in a sense where you can see a quicker progress in your body. Like, it is more effective on the body.

Yes

Yes, I mean in the upcoming researches that the researchers are carrying out they could maybe try and come up with something more feasible, something more effective which gives a faster result. Yes.

Yes, yes. That is the difficult thing

It is very frustrating as a patient using it and being, you know, hearing robot. You are thinking, "Ok this is something that is actually designed to, you know, do help" and it...you should see quick progress and quick improvement.

So you would have liked to have seen faster progress?

Yes faster progress.

Right but you have seen some progress?

I have

Good. Did you find it enjoyable to use?

Some days yes I guess. Some days it can be a **bit boring**. It all depends on your mood as well because if you are going to be like “Ok whatever” it is going to be “Ok whatever”.

Yes it is going to be a boring day.

Yes some days it is really enjoyable because like, you know, you are **using your actual**...It is like it is somewhat similar to, I would say in my version, is a Wii because you **are actually interacting with your hands on**. You are just testing how much you can score or what your best score can be, you know? Just trying to get it right.

Yes, that idea of it being like a computer game is something that we want to advance and make it a little bit better. But first can I get your opinion on what did you think of the graphics?

It is **very minimal** but I think they can give you a bit more to look at.

Ok

It can be a **bit boring** just looking at this screen with just this red thing on the screen. Yes, it can be a bit **boring**. There could be a bit more to look at, a bit more to be, you know, even could

maybe possibly use creatures, like little creatures running around and trying to get them. You know, stuff like that.

Yes, yes. Did you understand what you needed to do from the graphics? Did it make sense to you?

Yes it did.

It did, good. So you were able understand them but they were just a bit basic and a bit boring

A bit basic yes.

Would you like to have more interesting games incorporated into it?

Incorporated into it, yes definitely.

Did you find the scoring system, did that help in terms of monitoring your progress.

Yes

Yes?

Definitely for me because I am a bit competitive so definitely

So it was good to feel the scores getting better?

Yes, getting better and better

Did you find the movements challenged you?

Yes definitely because I even had a discussion with the actual person who supervised the sessions.

Yes

Right and I had said to him that some of the tasks are for more advanced people, you know like the grasping because if you don't have that much range of movement in your hand there is no way you can do that because it is going to be frustrating for you as a patient because, you know, it is asking you to do this but you are trying to do it and it is not happening. So it is really frustrating sometimes, yes.

Did you find that the reaching movement was easier for you?

The reaching was easier for me.

What about the turning over movement?

Rotating task, that was a bit challenging too.

Ok. That is a good mix of there still being something that you can use to work on...

Yes the good thing about it is that it can be monitored in you know, for such advanced or beginner depending on the range of movement you have in your hand. But it can get a bit frustrating if you don't have that much range of movement in your hand.

Yes, you mentioned earlier about it, making it more user friendly

Yes

What would you like me to do with it?

Well user friendly in the sense that maybe you **could get yourself set up** and you know get going if **someone is not there to** supervise you, to put you in.

I think that is key to it, that we need to simplify the set up

Simplify the set up, yes

In terms of computers, are you pretty computer savvy? Are you used to using computers?

I am used to them

Yes great, so you wouldn't have a problem with the interface of a computer?

No it is just the actual set up of the

The physical...

Yes, it is all a bit complex, you strapping yourself in and all that.

And it is hard to do with a weak, with a weak arm. Do the movements that you were doing, so the reach, rotate and grasp, do they seem meaningful or functional?

It was meaningful because these are things that we do in daily life activities, the hand is quite complex. It flexes, it adducts, it rotates.

Did you feel those movements you were practicing on the robot, did they tie in with your goals, with your rehab goals?

They did

Good

They did because to be honest I have **seen big change improvements in my hand.** It is actually doing much more so I am happy for that.

Good. Did you find the set up comfortable or did it cause you any pain?

Just a bit but I think it had to do with sensation problems.

Ok

Yes, within the palm of my hand. It was **just a bit uncomfortable**

So is the palm of your hand a bit hyper sensitive?

Hyper sensitive, yes

Ok and then when you put your hand and strapped it in that irritated it?

Yes it was just resting against it

You didn't get any shoulder pain from it?

No

Good, that's great. How about the length of time that you were using it for, how long did you use it for in general?

I would possibly say, off the top of my head I would say maybe three weeks

Yes, and in each session, were you using it for 10 minutes, 20 minutes, 30 minutes?

Maybe 10-15 minutes

Yes, was that long enough?

It could be longer

You...

But as I said before you don't want to have the sessions too long because sometimes it gets a bit **boring**, yes. And it is **frustrating** for you as a patient when you are trying to do something and it is not happening.

Yes and it is more the boring and the frustration than being too tired to keep going with it?

The **frustration**

Yes, so fatigue was not really a problem?

No fatigue was not a problem, it was just frustration and not being able to carry out the task being asked.

Ok. Did you find that you were able to maintain your concentration, your attention, while you were doing it?

Yes, definitely

Unless you got too bored?

Yes, unless you got **too bored**. I mean you have the screen in front of you and you know it is just basically you are watching so I was thinking if you had more characters or you know things on the screen.

Something like the Wii...

Yes, just to have **something more entertaining** going on in front of you that would just have your attention.

And that would keep you more in a...?

To keep you focused, engaged.

And then you might feel like using it more often?

A bit more often because it is funny using it

So having something that is fun, interesting and engaging...

Engaging

Would be a priority for you?

Definitely

Great, that is what we, that is what we want to develop in it. The other thing that we want to do is make the robot suitable for use at home. What would you think, sort of, if I offered you, I can't at the moment, but if I could offer you a robot to take home with you? Is it something you would be interested in?

As I said the set up is a bit complex. First you would have to know how to set it up.

Would you have somebody at home that would help you?

Definitely

You do, good. But you would need assistance to get set up. How about the size and space, would you be willing to make some space?

Yes the size is a bit, yeah. **Just a bit huge.**

We would need to make it a bit more compact.

More compact, yes. That is it.

That makes lots and lots of sense. Can I just go back? Where there any other movements that you would like to incorporate into it? Into the robot?

Well, no because I think that is basically it, reaching, grasping, rotating, that is what the arm does. It hyperextends, it flexes so...

You felt it covered the key movements?

I felt it covered the key movements of the arm.

I meant to talk more about the robot at home. The way that we envisage using it, some other robots have been set up like this, whereby you link the robot and the software that runs the robot is linked by the internet to me in a central clinic so that I can use, what do you call it? A webcam to watch you doing your exercises and I can monitor your progress so that your robot sends me feedback reports as to how often you are doing it, whether you are getting better at it, whether I need to turn up the intensity a little bit. Those kinds of things. What do you think of that as an idea?

It is a great idea but I don't think it would be as feasible as having the machine there because it is a hands on thing and having it at **home would actually help**.

This, you would have it at home. So you would have the robot connected to your computer, so it would be just like using it here but the idea behind it is that it would save me having to travel out to your house.

Ok

Yes, or save you having to come into the hospital. So that you would be able to practice it at home.

Not bad of an idea, but I mean monitored over the internet there are a lot things that you can do because you are concentrating on your posture, you are concentrating about your truncal strength, using your body to reach

Yes

You are using your arm. You know there are a lot of things you have to concentrate on. So having **someone who will monitor you** actually in the space I think is a better idea than being monitored over a webcam. Because you could be cheating using the wrong muscles and all that.

Exactly. I think we find lots of people do the lean forward instead of doing a nice reach from their arm. Yes that is good if you can identify the cheating postures then that is half the battle. Compared with your regular physio how useful did you find the robot?

I should say average.

So it is not amazingly better than your physio, than your regular physio but it is not..

It is average

Average, ok that makes sense.

If it was an actual, **an actual physio you get a lot more feedback** and you actually get hands on like massages and stuff, you know hands on stuff with actual physios.

And you can't replace that with a machine?

Right with a machine

And the idea behind the machine is to supplement physio not to replace it but to give you the repetitions of the movement because we know that repetitive task specific practice which is what the robot gives you is the optimum thing after brain injury or stroke. So that is the idea of it. Once you go home would you be interested if I had the robot set up in out patients here? Would you be interested in travelling in to use it?

Yes definitely

Yes, it would be something that you would value?

Yes

Or that you would consider would be worth your time, good, good.

If you **were progressing** I would definitely enjoy it. If I can see where I was benefiting definitely worth my time

Do you feel that the robot has contributed to your recovery?

Yes.

Ok, good. Is there anything else that you would change about the robot?

As I said its size, a little bit more compact and a little bit more user friendly.

Yes

Graphics, games

Yes, those are...

A little bit more interesting, a little bit more playful.

What kind of games would you like to see on it? What we are thinking of are the sport types of games...

Something just a little bit more entertaining. Something more, everyday activity because we are humans and you know we use our hands to do everyday activity, tasks that we are the brain is actually familiar with, things that you know can be remembered using the arm. It can be all like, you know send signals and stuff to that affected area.

One of the things that some researchers are looking at with robotics is using virtual reality with the robot. So that you have sensors on your hand and some of them have you know curved screens, large curved screens, and some of them have goggles and

eye pieces. But instead of playing a game you have an avatar or an image of your hand so that when you open and close your hand in the robot in your virtual environment you can do things with your hand. That means that you can do practical things with your hand so you could, I don't know, practice using a screwdriver or that type of, something that is real.

Yes real

Do you think that, which would you prefer to do games that are fun or to do the type of virtual reality thing which is more functional?

Virtual reality definitely. It is more functional, just more yes.

I think it is very high tech and the equipment is huge and bulky at the moment so we need to wait for some better advances in that technology before it is realistic, I think because our idea is to have something small, cheap, portable and easy to use. Is there anything else you want to tell me about the robot?

That is pretty much it.

It's pretty much it?

Yes

That is fine. Thanks for taking the time to have a chat with me.

